

ARCHIVES OF DISEASE IN CHILDHOOD

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DWARFISM WITH RETINAL ATROPHY AND DEAFNESS

BY

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The two children with this dystrophy, a girl aged seven years and eleven months and a boy aged six years and three months were admitted to the Hospital for Sick Children, Great Ormond Street, in June, 1935. The parents, who are natives of north Hampshire, are of English race, normal and not blood-relations, and they have been unable to trace the occurrence of the condition in their ascendants or collaterals. Dr. N. F. Kendall, under whose care they were before admission, has ascertained that before marriage the parents lived sixteen miles apart, and as their families have lived in the neighbourhood for a long time it is not unlikely that there has been inter-marriage between them some generations back. There are four older children, three girls, aged eighteen, fifteen, and twelve years respectively, and a boy, aged ten, and one younger, a boy aged three years, who is taller than either of the affected ones. The dwarfs are so much alike in facial appearance, build and disposition, that the same general description will suffice (fig. 1, 2). Both have small heads, that of the girl being the smaller (fig. 3), but, although the vault of the skull is flattened and the circumference small, the general shape is normal, and neither child has the receding forehead characteristic of microcephaly. Their faces are small with sunken eyes and prominent superior maxillae. They are slightly built with short, slender trunks and unduly long legs, and their feet and hands are too large in proportion. The third and fourth fingers of their hands are deviated a little towards the mesial line.

Both are active and their movements are quick and bird-like. They are friendly and playful, invariably good tempered, and laugh with obvious enjoyment at the slightest provocation. Although they are imitative, they have a certain amount of initiative and in playing with toys are no more destructive than most children of their age and class. They frequently make noises which at first sound like speech, but actual words can seldom be recognized, although the girl has been heard to say 'mother' and 'do it again' and the boy has said 'doctor' several times. They do not answer to their names or obey spoken words nor do they take any notice of a sound made behind their heads, but they are quick to obey signs. Mr. James Crooks, F.R.C.S., who saw them, says that although not totally deaf, their hearing is greatly impaired. It is difficult to tell how much of their backwardness is due to deafness and how much to mental deficiency. Their

behaviour is not the usual behaviour of deaf children. They appear to be a little below the average in intelligence and are far more excitable and laugh much more readily than children of normal mentality whether deaf or not.

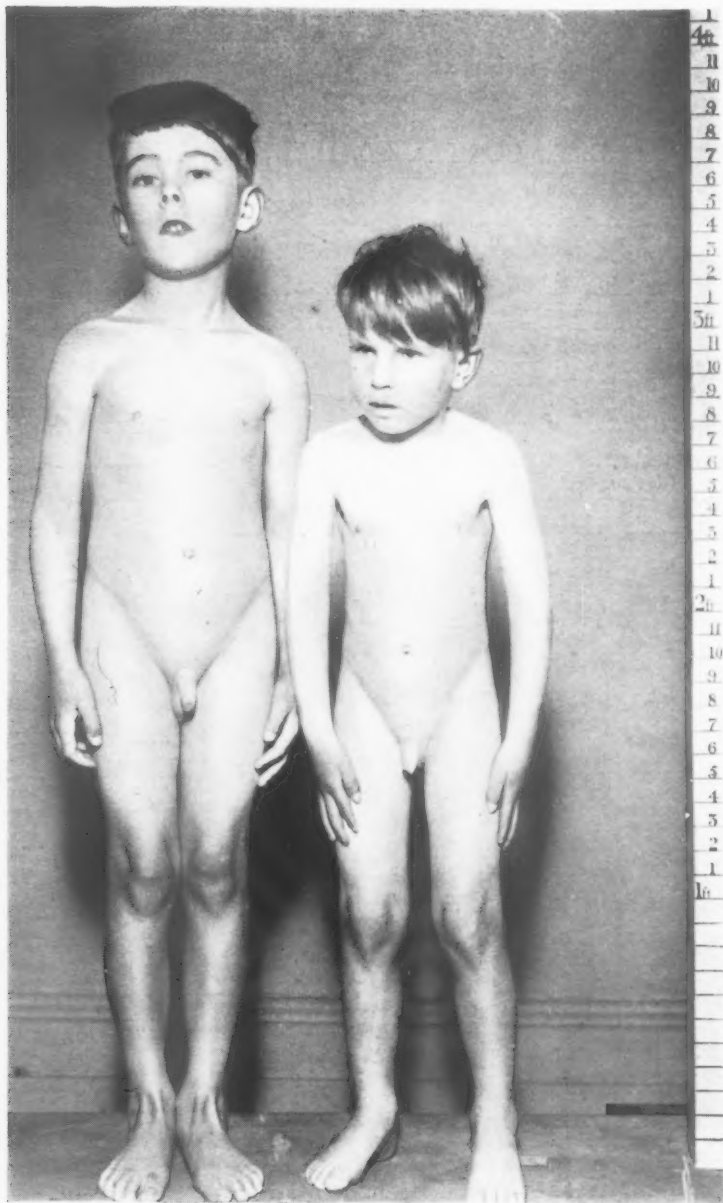


FIG. 1.—David D. with boy of same age.

Both have a scaly, erythematous dermatitis on the dorsum of the hands and wrists, on the legs, and on the face and ears, which according to the mother is worse after exposure to sun or wind, and their hands and feet are cold even in hot weather. Dr. R. T. Brain considers that the rash is trophic.

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X-ray pictures of the skeleton show that their skulls are similar in shape with the vault low, but in the girl the vault is greatly thickened (fig. 4), whereas in the boy it is only a little thicker than normal. In the girl the

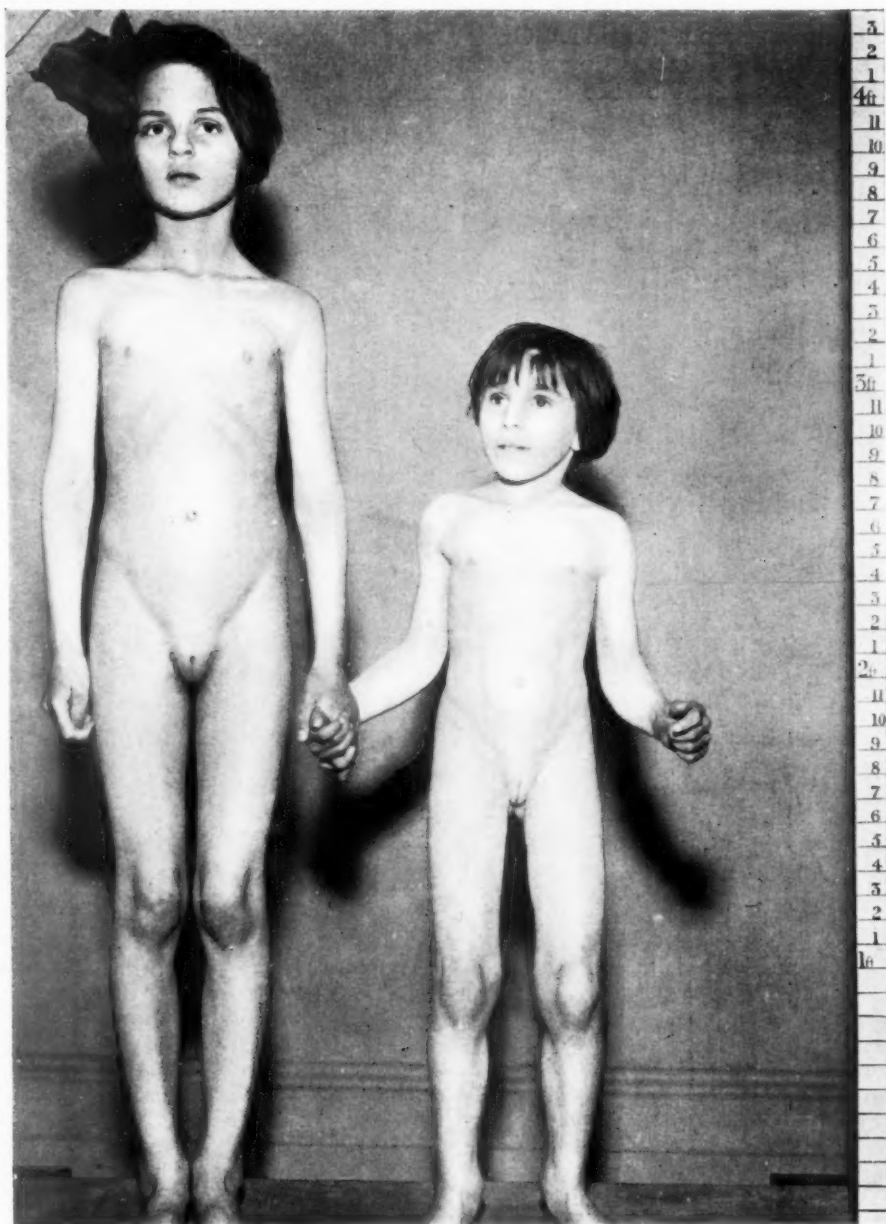


FIG. 2.—Pearl D. with girl of same age.

floor of the pituitary fossa is raised in the middle, and in the boy it is of the normal shape, but in both the fossa is unusually small. The vertebrae, long bones, and the bones of the hands and feet are of normal conformation and density in both children.

Appearances of the Eyes.

Mr. Arnold Sorsby, F.R.C.S., has kindly carried out an ophthalmological examination of the children and written the following report:—

THE EXTERNAL APPEARANCES of both children show that the eyes are normal in size and position. Ocular movements are full. Parallelism is not disturbed. There is no nystagmus. The globes appear to be sunken, probably as a result of the prognathism of the superior maxillae.



FIG. 3.—Pearl D. Head.

THE MEDIA are clear.

THE FUNDI show the following (fig. 5):—

DISCS. Considerable atrophy of the waxy type seen in retinal optic atrophy.

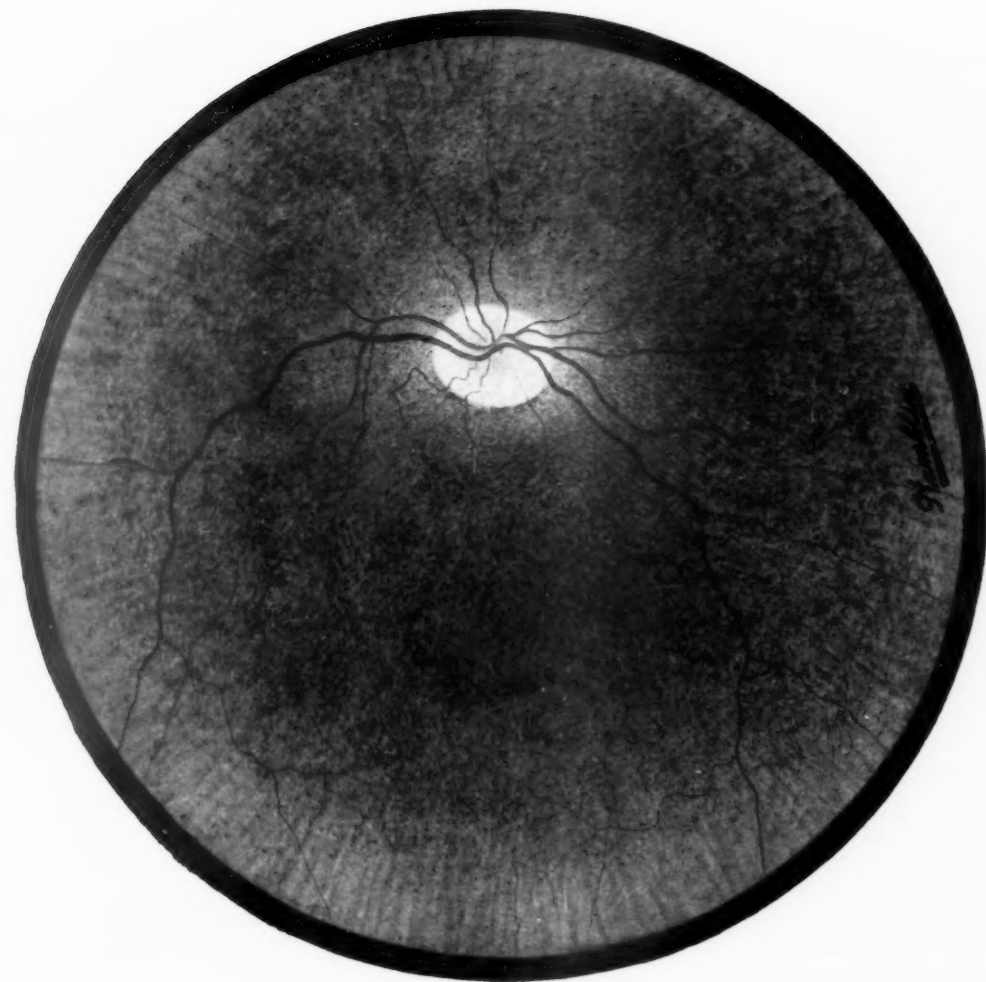


Fig. 5 (a). Pearl D.

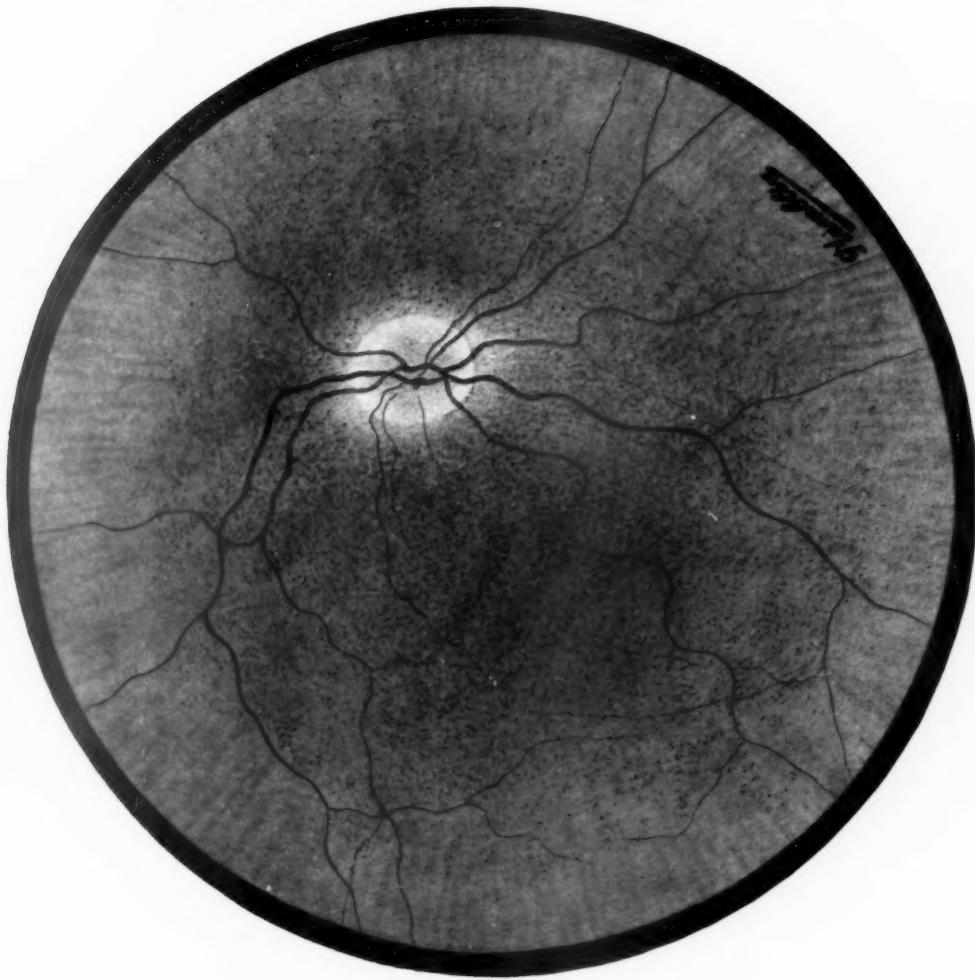


Fig. 5 (b). David D.

Dwarfism with retinal atrophy.



VESSELS. The arteries markedly narrowed, and veins are hardly affected. The background is dull-red in colour. The choroidal pattern is not seen. The macular reflex is absent. Scattered all over the fundus, but particularly aggregated towards the central areas, are a number of fine blackish dots like those seen in 'salt and pepper fundus,' but differing from the classical picture in the distinct and symmetrically heavier involvement of the central areas. Nowhere does the pigmentary disturbance tend to follow the blood vessels.



FIG. 4.—Pearl D. Skull, small, with thick bones.

The appearances in the two children are identical, except that the pigmentary disturbances are greater in the case of the boy.

The fundi are characteristic of extensive retinal atrophy with scattering of pigment. The absence of any definite choroido-retinal lesions and the symmetry would exclude congenital syphilis, the only condition requiring differential diagnosis from retinal atrophy. Their vision by day is good and they appear to have no night blindness, but no accurate test could be carried out. The visual fields could not be mapped out.

Detailed investigations.

The following is an account of details in the history, physical condition, and of investigations carried out on the two children.

Pearl D., seven years and eleven months, weighed $5\frac{3}{4}$ lb. at birth, started 'talking' at eighteen months, walked at three-and-a-half years. She has just started school, to which she has to walk two miles, but her attendance is irregular. Growth has always been slow. The appetite is poor. Her hair is dark brown, the eyes brown.

Height, 37 in. Weight, 27 lb. Circumference of head, $17\frac{3}{8}$ in.; of chest, $18\frac{5}{8}$ in.; and of abdomen, 17 in. Circumference of hands at base of thumb, 6 in.; length of hand, 5 in.; of arm, 17 in.; of foot, $6\frac{1}{2}$ in.; and of leg, 20 in.

The teeth comprise four lower incisors and two canines (second dentition), normal. Teeth of first dentition are carious.

W.R. negative; Kahn reaction negative.

Blood urea, 38 mgm. per cent.; non-protein nitrogen, 32 mgm. per cent.; cholesterol, 173 mgm. per cent.; blood calcium, 11.9 mgm. per cent.; and blood phosphorus, 3.9 mgm. per cent.

Fasting blood sugar, .078 per cent. After 5 minims of adrenalin the blood sugar figures were:—

After 20 minutes142 per cent.
„ 40 „108 „ „
„ 60 „107 „ „

UREA EXCRETION (urea concentration test).

			UREA	VOL. OF URINE
			PER CENT.	C.C.
Before urea	2.65	68
After 1st hour	2.24	8
„ 2nd hour	2.42	18
„ 3rd hour	1.52	21

David D., six years and three months. Weighed $8\frac{1}{2}$ lb. at birth. He stood at two years and walked at two-and-a-half years. He had only become clean in habits ten months before admission. He has always grown slowly. The testes are undescended, and the penis is of normal size. The hair is light brown and the eyes blue.

Height, $37\frac{1}{2}$ in. Weight, 39 lb. Circumference of head, 19 in.; of chest, 20 in.; and of abdomen, $18\frac{1}{2}$ in. Circumference of hand, 6 in.; length of hand, 5 in.; of arm (shoulder to tip of middle finger), $16\frac{1}{2}$ in.; of foot, $5\frac{1}{2}$ in.; and of leg (external malleolus to anterior superior spine), $18\frac{1}{2}$ in.

Teeth (first dentition) are carious, but otherwise normal.

W.R. negative.

Blood urea, 38 mgm. per cent.; plasma albumin, 4.18 per cent.; globulin, 1.93 per cent.; fibrin, 0.33 per cent.; total nitrogen, 6.44 per cent.; non-protein nitrogen, 32 mgm. per cent.; blood cholesterol, 198 mgm.; calcium, 11.3 mgm.; phosphorus, 4.3 mgm. per cent.

Fasting blood sugar, .072 per cent. After 5 minims of adrenalin the blood sugar figures were:—

After 20 minutes093 per cent.
„ 40 „124 „ „
„ 60 „121 „ „

UREA EXCRETION (urea concentration test).

			UREA PER CENT.	VOL. OF URINE C.C.
Before urea	4.45	80
After 1st hour	4.80	12
„ 2nd hour	3.46	17
„ 3rd hour	3.49	16

Discussion.

I have been unable to find a report of any similar case, and Mr. Sorsby, who is well acquainted with the literature of developmental and degenerative conditions of the retina can give me no reference to a parallel case. The condition seems to be most closely akin to retinitis pigmentosa with deafness, but, though the deafness in this syndrome varies from partial deafness to deaf-mutism, the retinal changes are different. In Usher's¹ series of cases pepper-like pigmentation was present in a few, but was accompanied by moss-like pigment or by the more typical pigmentation like bone corpuscles in shape. Even in these cases, no. 7, 12, 13, and 24, where there was more than one affected child in the sibship, the pepper-like pigmentation was only present in one sib, that in the others being typical, and in two of these families there was no deafness associated with the retinitis pigmentosa. Julia Bell¹ in her monograph in the *Treasury of Human Inheritance* includes a family with two affected members reported by Dering (no. 180). The fathers were brothers and the mothers were aunt and niece. One cousin had diffuse pigmentation reaching to the papilla, the retinal vessels were narrowed, and there was a posterior polar cataract in each lens. In the other cousin there were streaks of pigment in the retina. Hepburn² describes a brother and sister with retinitis pigmentosa and no deafness. In the brother most of the pigment was of the peppery variety, though typical masses shaped like bone corpuscles were present also. The brother had cold hands and feet and the sister had cold hands, but no mention is made of any dystrophic condition of the skin.

Nettleship³ in his comprehensive paper, for which he consulted the early literature in addition to analyzing his own long series of cases of retinitis pigmentosa, gives a list of anomalies found in association with it, but dwarfism is not amongst them. Julia Bell in her monograph also mentions all the abnormalities that have been found in people with retinitis pigmentosa. There is no case of dwarfism or reduction in size with increase in thickness of the skull, but cold hands and feet are mentioned by a few authors. Mental deficiency is not uncommon, but people with retinitis pigmentosa who are mentally deficient are usually feeble minded or dull, and if they have any alteration in temperament they are morose. Thus their mentality is very unlike that of these two children.

Retinitis pigmentosa with deafness resembles the syndrome described in this paper not only clinically but also in its familial incidence, and is inherited as a recessive, since 40·2 per cent. of the cases have consanguineous parents. It is rare, for only 3·3 per cent. of Nettleship's cases of retinitis pigmentosa were associated with deafness and only 4 per cent. of deaf-mutes out of 1,229 institutional cases were found to have retinitis pigmentosa. In some respects the syndrome resembles juvenile amaurotic idiocy but the pigmentation of the retina is more uniform and widespread, the mentality is different, and dwarfism has not been found in association with amaurotic idiocy.

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3. Nettleship, E., *loc. cit.*, 343.
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THE VALUE OF OESTRIN FOR PREMATURE BABIES

BY

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Following the suggestion made by Aschheim¹ in 1927 that premature babies might be beneficially influenced by the administration of oestrin there have been numerous papers on the subject, especially in the German literature. The results have been conflicting and when good effects have been claimed it is not always clear that adequate attempts have been made to secure proper controls for comparison. In 1933 Dr. A. N. Macbeth of the Organon Laboratories suggested that the work should be repeated in this country and a supply of 'Menformon' was kindly offered for this purpose. This was administered to certain premature babies as described below. At the same time, while in receipt of a personal part-time grant from the Medical Research Council, the author undertook a more extensive trial of two preparations of oestrin supplied on behalf of the Medical Research Council by British Drug Houses, Ltd. In respect of this trial guidance was afforded by Dr. A. S. Parkes concerning dosage, the type of preparation and the solvent used.

The arguments in favour of administering oestrin to premature infants are based upon the fact, mentioned by Martin², that the blood of new-born babies contains a comparatively large amount of oestrin. This is rapidly excreted by the kidneys and ceases to be present in the urine after about four days. It is argued that the baby born before term is at a disadvantage because it lacks the stimulus of the oestrin which would have continued to abound in its blood until the full term of pregnancy had the foetus remained in utero. The absence of this stimulus is held to be responsible, at any rate in part, for the drowsiness and general depressed condition of metabolism which constitutes the major handicap of the premature baby in the early days of life. The administration of oestrin, according to its advocates, remedies this deficiency and thereby enables the premature infant to gain weight and

improve its state generally in a more satisfactory way than the untreated infant.

Previous work.

This claim can now be examined by means of a brief critical review of the literature.

Martin² appears to have been the first to publish, in 1929, any account of clinical trials and he claims to have been working at the subject independently of the suggestion made by Aschheim, referred to above. He used an oily suspension of oestrin, sweetened by saccharine and gave it by the mouth to infants weighing less than 2 kgm. in doses of 100 mouse units (M.U.) per kgm. He first treated eight babies beginning on the fourth day (the day when the urine normally became free from oestrin) and claimed a steady rise in weight after a preliminary fall for one to two days, all of the babies developing in a manner more like full-time infants than prematures. A further series of eight premature infants were treated from the first day of life and they showed no loss of weight. No contemporary controls were used in assessing the results. Reiche³ in the following year reported the use of 'unden'—an oily solution of oestrin—for thirty-two premature infants and he compared the results with those obtained in his clinic for the preceding ten years, mainly basing his conclusions upon mortality rates. He claimed that for infants under 1200 gm. the mortality was reduced from 84.5 per cent. to 20 per cent.; for those weighing between 1200 and 1500 gm. the reduction was from 59 to 14.3 per cent.; for those between 1500 and 2000 gm. the reduction was from 47 to 33 per cent.; and for infants over 2000 gm. there was no appreciable change. All the deaths in the series occurred in the first week. The same dosage (100 M.U. per kgm.) was used as by Martin. Schiller⁴ used a purer preparation, namely folliculin, and he gave it by injection generally in a dosage of 20 to 40 M.U. daily, although in some cases improvement was claimed from a daily dose of only 4 M.U. In all, sixty-eight premature infants were treated and it is claimed that a notable effect was obtained in the shape of steeply rising weight curve, usually after only a small preliminary loss, often regained on the second day. If the injections of oestrin were stopped or decreased the rise in weight was noted to be arrested. MÜgel⁵ used 'unden' given by the mouth (100 M.U. per kgm.) for thirty-nine premature infants. The results obtained were compared with the progress made by untreated infants, all being under the control of the same nursing-sister. In all weight groups better progress was made by the treated babies. The records, however, with two exceptions, refer to babies over 2000 kgm. (approximately 4 lb.) and deal with progress for only ten days. Nölle⁶, in reviewing the subject of female sex hormones, mentions the use of 'progynon' for two premature babies in a daily dose corresponding to approximately 125 M.U. with good results. Kulka⁷ used 'unden' by the mouth in doses of 100 M.U. per kgm. daily for thirty-seven premature infants and his impression was that better gain in weight was seen than usual. There were no controls for this series. Schreiber⁸ reports a much better controlled series of cases. He treated eighty-five premature infants with 'unden' and compared the results with those of a previous series of premature infants of similar birth weight. There was no distinct difference in mortality and morbidity for the two groups but the weight curves showed a definite advantage for the

treated cases. The infants receiving hormone gained 0.4 per cent. of their birth weight in the period of observation (eleven days on the average) while the untreated cases had lost 2.4 per cent. In ten pairs of twins there was an even more striking difference in favour of the treated infants. Schreiber employed the usual dosage of 100 M.U. per kgm. but he suggests that bigger doses might have yielded even better results. Brochier⁹ reports similar good results as regards gain in weight using four drops daily by the mouth of a solution of 'folliculin' containing 1000 international units (I.U.) per c.c. (The relation of M.U. to I.U. is discussed below.) This means approximately 250 I.U. daily. Brief reference to similar investigations with various ovarian hormones is also made by Devraigne and Sauphar¹⁰, Nobel¹¹ and Bernheim-Karrer¹². The last-named considers that on the whole the development of premature infants treated by 'unden' was no better than that of untreated babies.

Another method of using oestrin for premature babies has been to employ the blood or serum of pregnant women which is rich in ovarian hormone. Estimates of the dosage thus employed suggest that approximately 1 to 10 M.U. of oestrin was given daily either by injection or by the mouth. Beneficial results are claimed by v. Oettingen¹³, v. Raisz¹⁴, Schwartz¹⁵ and Unbehaun¹⁶. Siegmund¹⁷ points out that the serum of pregnant women also contains prolactin and he thinks it improbable that the good results obtained are due solely to the effects of known hormones.

Against these results, either with a preparation of oestrin or with the serum of pregnant women, Stork¹⁸ speaks strongly stating that he has seen no uniform good effects. With 'unden' in twelve premature babies (100 M.U. per kgm. daily for seven days) there were no beneficial results obtained. This author also experimented with 'prolactin' but abandoned this because of disturbing symptoms. Edelstein¹⁹, who used injections of serum from pregnant women, also failed to find any beneficial effect.

The main impressions gained from the survey of the literature here summarized is that with certain exceptions the results reported are uncontrolled and too much emphasis is laid upon relatively slight evidence that treated infants made better progress than untreated babies. Few details are given as to other conditions, all of which are important for the premature baby, such as nursing, room temperature, and nourishment in particular.

Present investigation.

Any scientific attempt to assess the value of oestrin or any other form of treatment for premature babies must inevitably base its results upon mortality and morbidity rates and comparison of weight curves. The criteria for assessing the progress in premature infants have been set out elsewhere²⁰ and while the factors concerned are numerous and complex it is generally agreed that nursing care plays a dominant part. It follows, therefore, that any controlled investigation concerning premature

infants must have constant conditions as regards nursing care and it is preferable that as far as possible the nurses concerned should be unaware which infants are receiving treatment and which are controls. This can best be achieved by the use of inert solutions for the control babies. This has, in fact, been carried out in the present investigation. Over a period of approximately two years, premature babies—that is to say babies weighing 5 lb. and under—born at Queen Charlotte's Hospital have received either treatment by oestrin or injection of the inert solvent solutions used for the oestrin. Alternate babies received either one or the other and in the case of twins of the requisite weight one received oestrin and one received the control solutions. The arrangements at the hospital are such that each of the three floors has a side room in which small and ill infants can be nursed apart from mothers and other infants. The arrangements as regards room temperature, the degree of humidity and methods of general hygiene and feeding are more or less constant throughout the hospital and all the babies have been supervised by the author. It will be seen that in this way valid contemporary controls have been obtained. In no other way can conditions be kept the same for a control series and it is useless, as some of the authors quoted above have done, to compare a treated series of babies with a previous group when there is no guarantee that all conditions will have been the same.

As will be seen below, when results are discussed, general mortality and morbidity rates give very little help in assessing the value of special forms of treatment since, where nursing skill is of a high standard, such rates are already remarkably low. Indeed, the experience gained during the past few years at Queen Charlotte's Hospital suggests that in expert hands the prognosis of the premature baby is remarkably good. If, however, it could be shown that any form of treatment improves the general condition of the premature baby, especially as regards promoting a steady gain in weight, it would be available for small babies in less favourable circumstances where it might turn the scale in their favour.

It is obvious that the gain in weight, which forms the basis of assessment in the results here reported, as well as in most of the previously published records, is dependent in main upon the fluid and food intake of the premature infant. This is governed by the skill of the attendant in inducing the infants to swallow and by the level of metabolism in the infant. In all the babies described in this series the methods of feeding were similar, the earliest 'feeds' offered being half-strength normal saline, followed by colostrum and dilute breast milk according to the stage and weight of the infant. In subsequent days undiluted breast milk and later a weak 'humanized' dried milk were used—the latter

only when insufficient breast milk was available. The quantities offered were governed more or less by the amounts which the babies would take. These conditions of feeding were the same for all the babies, treated and untreated, so that it may fairly be assumed that the only variable factor was the condition of the infants in the general state and level of metabolism. If it could be shown that treated babies gained weight better than untreated babies this could be attributed to the stimulant effect of the treatment. On this basis comparison of weights of treated and untreated babies has been used as the main criterion for assessing the results. It would be ideal for babies under observation in this way to be weighed daily but such procedure necessitates in some cases more disturbance and exposure than it is wise to risk. Consequently, while in general babies were weighed daily, this procedure was omitted if the child's condition did not seem good. It has been possible from the general trend of the weight curves to calculate the weight on the seventh day of life in the few instances when this was not available.

Dosage.—The literature suggests that a standard dose among Continental workers was 100 'mouse units' per kilogramme body weight. Schreiber⁸, whose work is quoted above, in the most convincing of the published records, suggested that bigger doses might give more clear-cut results. It was consequently decided to begin with 100 M.U. per pound body weight, giving the total amount by one injection daily to the nearest half-pound. The first injection was given during the first twenty-four hours but not necessarily at the same time for each baby, so that the period elapsing between severing the cord and the injection of oestrin varied from a few to nearly twenty-four hours. The first group of babies actually received this dosage in the form of trihydroxyoestrin ('oestriol') in olive oil in a strength of 1000 M.U. per c.c. The control infants received injections of olive oil. Ampoules containing the two solutions were labelled 'oestrin A' and 'oestrin B' respectively so that the nursing staff were unaware of which received oestrin. Six premature infants received oestrin and there were seven control infants during the same period. The next group received 'menformon' in aqueous solution (supplied as already mentioned by the Organon Laboratories) which is ketohydroxyoestrin ('oestrone') in a dosage of 100 international units per pound body weight, the controls in this group being given injections of the aqueous solvent. Seven babies received this oestrin ('C') and there were six control babies over the same period ('D'). Examination of the results so far obtained indicated clearly that much larger numbers were necessary to determine the value of oestrin for premature infants. More ketohydroxyoestrin was supplied in olive oil (from British Drug Houses

as already mentioned) and used in a dosage of 100 I.U. per pound of body weight (oestrin 'K') while control babies received injections of olive oil (oestrin 'J') as before. In this group thirty-one babies received oestrin and there were twenty-three controls. (It is difficult to explain why there were fewer controls as alternate babies received either 'K' or 'J.' The oestrin was supplied in ampoules containing 500 I.U. in 0.5 c.c. of olive oil and blank ampoules contained 0.5 c.c. of olive oil. Once an ampoule was opened its contents were either used at once or discarded. It might therefore happen that one ampoule supplied a daily dose for two babies or for one.)

It will be noted that apart from the six babies treated with 'oestrin A' (trihydroxyoestrin) the dosage was regulated in I.U. instead of M.U. as generally used in the literature summarized above. This change took place in conformity with the tendency among workers on other aspects of oestrin therapy and activity to discard the purely animal standards (rat and mouse units) in favour of the international unit. It would appear that one I.U. of ketohydroxyoestrin is about three to four times as active as one M.U. of trihydroxyoestrin, in so far as they are comparable. Thus the majority of the babies treated in this investigation received a very much higher dose of active oestrin than in any previously recorded study. To avoid confusion and to make the administration of the oestrin as easy as possible for the nursing staff no mention of the 'units' was made in this sense. Injections were made from insulin syringes in which 0.1 c.c. was represented as a two units marked on the barrel. Thus 2 'units' as marked on such a syringe was equivalent to 100 mouse or international units of oestrin.

Results.

Oestrin was injected as above described daily for the first seven days of life. This period was chosen partly as a result of what had been attempted elsewhere and partly because it was felt that any beneficial result would show itself during this period when the weight is tending to oscillate. The results given here are considered mainly under the headings of the weight on the seventh day and on the fourteenth day or earlier if the infant was discharged before this. There were so few deaths and so little general morbidity that no statistics are offered on these lines. Twins are considered separately and sex differences have been calculated for the third and largest group. During the period of two years that the investigation has been in progress there have been eighty babies under supervision whose records are analysed below. During the

same period there have been fifty babies who came strictly within the definition of 'five pounds or under' who did not receive oestrin. There was no deliberate exclusion of these babies but various circumstances combined to render them ineligible. Most of them were exactly or very nearly five pounds in weight, full-term infants who were nursed in the general wards, treated and behaving throughout like normal infants of full weight. In other cases the injections of oestrin were omitted on the first and second day and there seemed no point in complicating the clinical findings by including babies whose treatment was begun at varying periods. Babies dying on the first day of life did not receive oestrin. Two examples of gross abnormality were not treated (hydrocephalus and very large haemangioma). Four babies living for two days and one for four days were so ill from the start that oestrin was not given. Four infants receiving oestrin or control solutions died during treatment: one received one injection of oestrin A, and died on the second day of life, after repeated cyanotic attacks; one died on the thirteenth day, and is mentioned in Group I below; the other two were receiving control injections and died on the fourth and third day respectively (weights 1 lb. 8 oz., and 3 lb. 14 oz. (one of triplets)). As far as possible the author saw every baby as often as was necessary (usually twice to three times weekly) and during holidays certain of the premature infants then born were also omitted from the investigation.

Group I. Oestrin 'A' and 'B.' Six babies received 100 M.U. of trihydroxyoestrin in olive oil per pound weight, by subcutaneous injection daily for seven days, and seven contemporary controls received olive oil only.

TABLE 1.

	AV. WT. AT BIRTH.	AV. WT. SEVENTH DAY.	AV. WT. FOURTEENTH DAY.
'A' SERIES (TREATED) ...	4lb. 2oz. (3lb. 14oz.)	4lb. 5oz. (4lb.) ...	4lb. 1oz.
'B' SERIES (UNTREATED)	4lb. 6oz. (4lb. 4oz.)	4lb. 4oz. (4lb. 2oz.)	4lb. 6oz.

Figures in brackets show average for 4 babies in 'A' series and for 6 babies in 'B' series who were weighed on fourteenth day.

Of babies receiving 'A' all did well except one who died on the thirteenth day of life with pneumonia. It appeared that his condition deteriorated after the oestrin was stopped on the seventh day. Four babies of this group were completely breast fed and two received mixed feeding (breast milk and modified cow's milk). The highest weight at

birth was 4 lb. 13 oz., and the lowest 3 lb. 5 oz. Of babies used as controls all did well, six being completely breast fed and one receiving mixed feeding. The highest weight at birth was 4 lb. 14 oz., and the lowest 3 lb. 10 oz. There were no twins for comparison in this group. The results show a slightly better weight gain for the treated babies, but the numbers are small.

Group II. Oestrin 'C' and 'D.' Seven babies received 100 I.U. of ketohydroxyoestrin (menformon) in aqueous solution per pound of body weight, by subcutaneous injection daily for seven days. Six contemporary controls received the aqueous solvent only.

TABLE 2.

	AV. WT. AT BIRTH.	AV. WT. SEVENTH DAY.	AV. WT. FOURTEENTH DAY.
'C' SERIES (TREATED) ...	4lb. 3oz.	4lb. 1oz.	—*
'D' SERIES (UNTREATED)	3lb. 15oz.	3lb. 15oz.	4lb. 5oz.

* All babies receiving 'C' except one were discharged before the fourteenth day.

Of babies receiving 'C' all did well throughout except one weighing 3 lb., who developed fever on the fourth day, but quickly responded to extra fluid. All seven babies were breast fed. The highest weight at birth was 4 lb. 12 oz., and the lowest 3 lb. Of the babies used as controls, four did well throughout, one developed oedema and recovered, and one collapsed on the eighth day, but recovered. Four were breast fed and two received mixed feeding. The highest weight at birth was 4 lb. 12 oz., and the lowest 2 lb. 8 oz. One set of twins, both girls, responded as follows :—

	Av. wt. at birth.	Wt. seventh day.	Av. fourteenth day.
TREATED 'C' ...	4 lb. 3 oz.	4 lb. 7 oz.	5 lb.
UNTREATED 'D'	3 lb. 14 oz.	4 lb. 1 oz.	4 lb. 6 oz.

Both were breast fed and there is no appreciable difference between their progress. The results for the other babies did not show any material difference except that those in the control series did not lose so much weight.

Group III. Oestrin 'K' and 'J.' Thirty-one babies received 100 I.U. of ketohydroxyoestrin in olive oil per pound body weight, by subcutaneous injection daily for seven days. Twenty-three contemporary controls received olive oil only.

TABLE 3.

	AV. WT. AT BIRTH.	AV. WT. SEVENTH DAY.	AV. WT. FOURTEENTH DAY.
'K' SERIES (TREATED) ALL BABIES	3lb. 14oz.	3lb. 12oz. (-3.2)	—
DITTO 27 BABIES REMAIN- ING IN HOSPITAL UNTIL FOURTEENTH DAY	3lb. 13oz.	3lb. 11oz. (-3.3)	3lb. 15oz. (+3.3)
'J' SERIES (UNTREATED) ALL BABIES	4lb. 1oz.	3lb. 15oz. (-3.1)	—
DITTO 17 BABIES REMAIN- ING IN HOSPITAL UNTIL FOURTEENTH DAY	4lb.	3lb. 13oz. (-4.7)	3lb. 14oz. (-3.1)

Figures in brackets show percentage increase or decrease over birth weight.

Of babies receiving 'K' all did well throughout except one who became deeply jaundiced and recovered after two injections (10 c.c.) of maternal whole blood. One died at eight weeks old from gastro-enteritis. (It should be noted that no subsequent follow-up of babies has been attempted.) Twenty-one were breast fed and ten received mixed feeding. The highest weight at birth was 4 lb. 14 oz., and the lowest 2 lb. 8 oz. Of the babies serving as controls all did well throughout except four: one was mildly jaundiced and lethargic, one developed oedema and recovered, one was very lethargic throughout and received thyroid extract as a stimulant after the fourteenth day, and one was very ill with cyanotic attacks and unexplained pyrexia, but recovered. Nineteen were breast fed and four received mixed feeding. The highest weight at birth was 4 lb. 12 oz., and the lowest 2 lb. 9 oz. It will be seen that by comparing the weights on the seventh day there is no material difference in the two groups, but by the fourteenth day the treated babies showed an average increase of 3.3 per cent. of their birth weight while the control babies were still 3.1 per cent. below birth weight. There is therefore a slight advantage in favour of the treated group. The two smallest babies in this group both did well, the details of their weights being as follows:—

	Birth wt.	Wt. seventh day.	Wt. fourteenth day.
TREATED ...	2 lb. 8 oz.	2 lb. 4 oz.	2 lb. 6 oz.
UNTREATED ...	2 lb. 9 oz.	2 lb. 4 oz.	2 lb. 8 oz.

Both received breast milk only.

There were six sets of twins in this group and two surviving babies of one set of triplets. The average weights of these fourteen babies are as follows, one of each set being treated :—

		Birth wt.	Wt. seventh day.	Wt. fourteenth day.
TREATED	...	3 lb. 15 oz.	3 lb. 13 oz.	4 lb.
UNTREATED	...	3 lb. 15 oz.	3 lb. 14 oz.	4 lb. 1 oz.

The untreated babies thus showed a slight advantage.

The results in this group have also been analysed for the two sexes. Very curiously thirty-three out of the fifty-four babies were females, a marked sex preponderance.

TABLE 4.

	AV. WEIGHT AT BIRTH.		AV. WEIGHT SEVENTH DAY.		AV. WEIGHT FOURTEENTH DAY.	
SEX & No.	M=11	F=20	M=11	F=20		
'K' SERIES (TREATED) ALL BABIES	3lb. 15oz.	3lb. 13oz.	3lb. 12oz. (-3.2)	3lb. 12oz. (-1.6)	—	—
SEX & No.	M=9	F=18	M=9	F=18	M=9	F=18
DITTO 27 BABIES REMAINING IN HOSPITAL UNTIL FOURTEENTH DAY	3lb. 13oz.	3lb. 12oz.	3lb. 10oz. (-4.9)	3lb. 12oz. (0)	3lb. 13oz. (0)	4lb. (+6.7)
SEX & No.	M=10	F=13	M=10	F=13		
'J' SERIES (UNTREATED) ALL BABIES	4lb. 2oz.	4lb. 1oz.	3lb. 15oz. (-4.5)	3lb. 15oz. (-3.1)	—	—
SEX & No.	M=8	F=9	M=8	F=9	M=8	F=9
DITTO 17 BABIES REMAINING IN HOSPITAL UNTIL FOURTEENTH DAY	4lb. 1oz.	3lb. 14oz.	3lb. 12oz. (-7.7)	3lb. 13oz. (-1.6)	4lb. 1oz. (0)	3lb. 12oz. -(3.2)

Figures in brackets show percentage increase or decrease over birth weight

Analysed for differences in the two sexes the results show a more or less uniform advantage for the treated babies, i.e., less loss of weight, for the first seven days, in both sexes, the females losing slightly less than the males throughout. At the end of fourteen days the differences are more striking, the treated and untreated male babies being just back to birth weight while the females show a 6.7 per cent. increase for the treated series and a decrease of 3.2 per cent. for the untreated series. It would seem that the advantages shown for the two sexes together in table 3 must be mainly attributed to improvement effected in the female babies.

Conclusions.

A controlled series of investigations concerning in all eighty premature babies shows that subcutaneous injections of oestrin during the first seven days of life in doses of 100 M.U., trihydroxyoestrin (oestriol) 100 I.U., ketohydroxyoestrin (oestrone) per pound body weight have a slight stimulant effect as indicated by a better gain in weight than in babies not so treated. This improvement is more obvious in girl babies than in boy babies. The advantages produced by the oestrin injections do not appear definite enough to warrant the use of this substance as a routine measure for premature babies.

Acknowledgments.

The credit for the good results obtained with the large number of premature babies forming the object of this investigation must go to the Nursing Staff of Queen Charlotte's Hospital and especially to the ward sisters. Help has been obtained on various aspects of the problem from Dr. A. S. Parkes, Prof. E. C. Dodds, Dr. A. N. Macbeth (of Organon Laboratories), and Mr. E. R. C. Edyvean (of British Drug Houses, Ltd.), to whom the author tenders his thanks.

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BLOOD VOLUME AND CIRCULATION TIME IN CHILDREN

BY

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This paper is based mainly on the results of the author's own research work on blood volume and circulation time in cases of normal and sick children. The following methods were used:—

1. **The colorimetric method** for determining the circulating plasma volume, and the haematocrit method for estimating the volume of the total circulating blood; and
2. **The histamine rash method** for estimating the minimum circulation time of the blood.

By means of these two methods there is determined only that portion of the total blood volume which is in rapid circulation, the other part, the so-called stored or depôt blood, which is moving slowly or is almost stationary, being neglected. The organs which may act as blood depôts are the spleen, the liver, the intestines, the sub-papillary plexus of the skin and possibly the muscles. The greater part of the capillary system of these organs is quite extensive enough to supply stored-up blood as and when required to the more rapid circulation or alternatively, withdraw rapidly circulating blood and store it. This action is regulated by the autonomic nervous system. The circulating blood volume as determined by the above methods is not absolutely fixed in quantity but changes within wide limits, according to the physiological or pathological conditions under which it is measured. At the same time the stored-up blood varies in the contrary direction, provided that the total volume of blood is not affected by external losses. In the latter case, the organs containing the stored-up blood strive to make good the loss of circulating blood by sending blood into the circulatory system.

Observations on healthy infants and children.

The amount of the circulating blood volume under normal conditions in children of all ages (excepting newborn babies) amounts to 8.3 (± 1) per cent. of the bodyweight, or 83 (± 10) c.c. per kgm. of bodyweight. The circulating plasma represents about 50 c.c. per kgm. of this total and the

circulating cell volume 33 c.c. per kgm. Relatively high values are found in the two periods of growth, i.e., between 3 and 6, or 11 and 13 years (about 90 c.c. per kgm). The normal figures for adults by the same method are 75 c.c. per kgm. of which 40 c.c. represent plasma and 35 c.c. cells. As age increases, the blood volume like other tissues becomes poorer in water, i.e., the proportion of circulating plasma volume is reduced and that of the circulating cell volume increased. (Cell plasma ratio in infants 39:61 per cent., in older children 42:58 per cent., in adults 45:55 per cent. Cf. the rise in haemoglobin and red cell figures). Chart 1 is based on these data. It can be seen how the circulating blood volume gradually increases with bodyweight and age; it is the only isolated 'organ' the increasing weight of which can be measured *in vivo*.

Movement, feeding and high outside temperature increase the circulating blood volume. If infants are given water to drink, there is to be observed half an hour to an hour later the so-called hydraemic reaction of the blood in the form of an increase of the circulating blood volume up to 15 per cent. of the original value with relatively higher increase of the plasma volume. The highest values to be found for the circulating blood volume under conditions of heat and bodily activity, are 11-12 per cent. of the bodyweight. If it is assumed that in such conditions the blood stores are almost empty, then the figure of 3 to 4 per cent. of the bodyweight, or 30-40 c.c. per kgm. can be deduced for the estimated size of the normally stored blood volume, that is about one-third of the circulating blood volume.

In chart 1, the circulation time at various ages is also recorded. It increases from 14 or 15 seconds in infants to 22 seconds at the age of 15. The average for adults is 23 to 30 seconds. What is measured by the histamine rash method is the 'minimum' circulation time of the swiftly moving particles in the axial current of the blood vessels. The average value for the circulation of all particles even the slowest moving—the 'mean' circulation time—must therefore be higher, and is estimated at about double the minimum circulating time, i.e., between 28 and 60 seconds.

The minute volume of the heart is calculated from the circulating blood volume and the mean circulation time of the blood (the ordinary methods of estimation are not applicable to children). The formula is as follows: Circulating blood volume in c.c. multiplied by 60, and divided by the mean-circulation time in seconds. The minute output of the heart therefore attains in infancy 165 c.c. per kgm. or $\frac{1}{2}$ to $1\frac{1}{2}$ litres, and changes slowly to the values at the end of childhood, namely 90 to 100 c.c. per kgm. or 3 to 4 litres (adult value 70 c.c. per kgm. or 4 to 5 litres by more direct methods). The slow decrease of the minute-output per kgm. of bodyweight as age increases goes parallel with the decrease of the basal respiratory

metabolism per kgm. In adults both are only about half as large as in infants.

The output per beat of the heart, found by dividing the minute volume by the pulse rate appropriate to the age, increases from 5 c.c. in the case of very young infants to 55 c.c. in the fifteen-year old child (adults 60 to 70 c.c. At the ages between 6 months and 21 years it fulfils the empiric formula $(3 \times n) + 8$, 'n' representing the number of completed years.

Newborn infants require a separate discussion. Here things have still a foetal character, the blood volume of the foetus being relatively enormous.

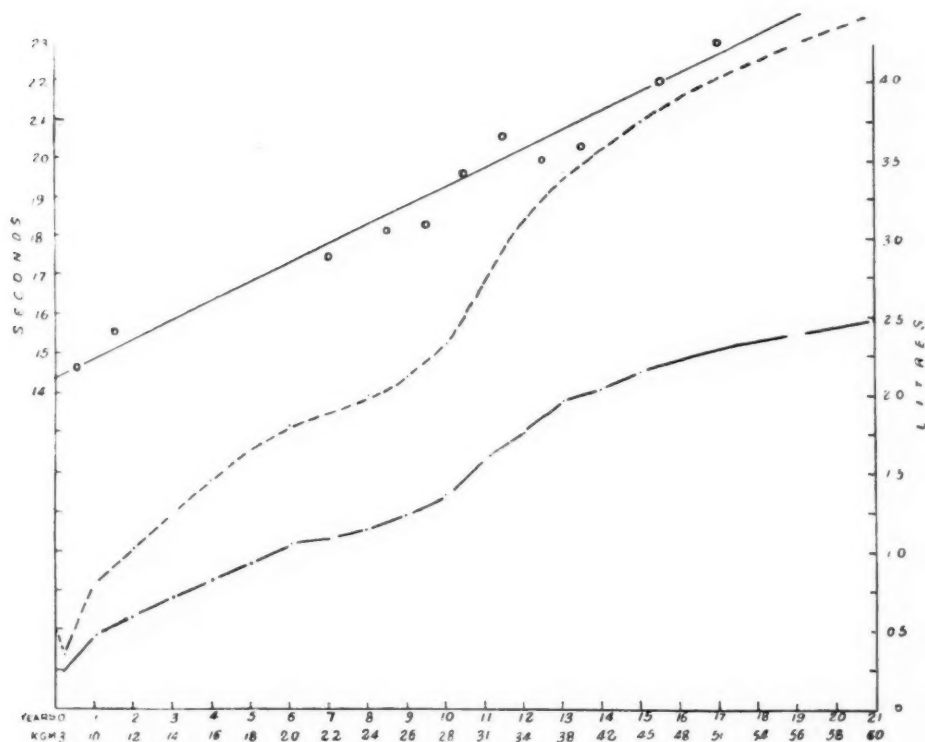


CHART 1.—Circulating plasma volume (— · — · —), circulating blood volume (— · — · —) and circulation time (° — — — °) from birth to 21 years. Average results.

At the beginning of development it surpasses even the embryo in weight by reason of the still quicker growth of the placenta; at the same time the blood is poor in haemoglobin. Towards the end of pregnancy, however, the blood becomes rich in haemoglobin and the blood volume decreases in proportion to the embryo-weight, but never below 10 to 15 per cent. of the latter. This is the exact figure found for the circulating blood volume in newborn humans. It varies according to the time of severing the umbilical cord, i.e., according to the size of the 'postnatal blood-transfusion' (up to 100 c.c. blood) between 12 and 15 per cent. of the bodyweight or 400 to

500 c.c. blood. The proportion of the circulating cell volume amounts to 55 to 60 per cent. of the blood volume, according to the richness in haemoglobin and red cells of the newborn infant's blood. The circulation time of this thick blood with high cell content can be prolonged, whereby the minute-output of the heart is kept within reasonable limits. During first weeks after birth, the haemoglobin and red cell figures decrease (haemoglobin from about 120 to 70 per cent., red cells from about 6 to 4 millions per c.mm.) and parallel to this the circulating blood volume decreases also, especially in its cell proportion (see chart 1). It decreases from about 500 to about 350 c.c., the proportion of the circulating cell volume amounting to only 35 to 40 per cent. The destruction of this amount of blood rich in haemoglobin is the cause of icterus neonatorum and physiological anaemia during the postnatal period.

Observations in sick infants and children.

(a) Polycythaemia and anaemia.

In those types of congenital abnormalities of the heart and the larger blood vessels, in which heart and circulation partly retain their foetal character, the two sides of the circulatory system are in communication with each other, venous and arterial blood partly mix and the haemoglobin and red cell values remain high. The blood volume condition of such children reveals high figures with a relative preponderance of circulating cell volume (table 1). (The cases marked with an asterisk are here published for the first time.)

TABLE 1.

VOLUME OF CIRCULATING BLOOD IN CASES OF MORBUS COERULEUS.

CASE	AGE.	WEIGHT KGM.	HAEMO- GLOBIN. PER CENT.	RED CELL MILLIONS. PER C.MM.	CELLS PER CENT.	PLASMA VOLUME. C.C.	CELL VOLUME C.C.	BLOOD C.C.	VOLUME. PER CENT. BODY WEIGHT.
3	1 mth.	3.5	135	8.50	64.9	150	295	445	12.7
148*	3 yr.	12.0	105	6.80	62.7	476	798	1274	10.6
220*	2 mth.	3.9	90	5.02	50.6	215	219	434	11.3

The cases of anaemia furnish a counterpart to those of polycythaemia from the haematological point of view. Such cases in children of 2 months to 2 years have been examined. The circulating cell volume is generally speaking as much decreased as the haemoglobin value; it varies between 7 and 23 c.c. per kgm. according to the intensity of the anaemia. The amount of circulating plasma volume shows differences. In the one group of cases—mostly constitutional types of anaemia—the plasma volume is also, although in a lesser degree, diminished (38 to 49 c.c. per kgm). The total circulating blood volume is therefore considerably less (45 to 63 c.c. per

kgm.). In the other group of cases, mostly of anaemia caused by infection, the circulating plasma volume is normal or even in a compensating degree increased (47 to 60 c.c. per kgm.). The result is a normal or only slightly diminished total circulating blood volume (67 to 81 c.c. kgm.). If the circulating blood volume is studied during the recovery from anaemia over a period of weeks and months (up to four examinations of one and the same child), it is possible to demonstrate the circulating cell volume increasing parallel to the haemoglobin curve and returning to normal. The circulating plasma volume in the one group also increases gradually; in the other generally decreases slowly, so that the total volume of circulating blood returns to the normal level. One example will suffice:—

Case No. 249. Infant, ten months old, with anaemia caused by an infection. Weight, 6.3 kgm. Haemoglobin, 40 per cent. Cells, 19.8 per cent. Plasma, 359 c.c. Cells, 79 c.c. Blood, 438 c.c. Eleven weeks later, after blood transfusion (100 c.c.). Weight, 7.1 kgm. Cells, 35.2 per cent. Plasma, 308 c.c. Cells, 166 c.c. Blood, 474 c.c.

The circulation time of the blood appears to be shortened in cases of anaemia (the histamine rash is often not recognizable on account of the pallor). For this reason the minute volume of the heart is brought up to the normal or is even above normal, and the oxygen supply to the tissues is maintained. In recovery from cases of anaemia in early childhood, unusually high demands are made on the bone marrow, inasmuch as it has not only to replace the lost blood, but to guarantee the normal increase of blood volume during the period of recovery in proportion to the growth of the body. Energetic therapeutic steps are all the more necessary—either in the form of diet, or iron treatment, or, in severe cases, by large blood transfusions.

(b) Collapse and shock.

Collapse or shock is characterized haemodynamically as a disturbance in the blood distribution, with a striking disproportion between circulating and stored blood volume. The former is considerably reduced, the latter is proportionately increased. The blood flow is slow, the minute output of the heart is small, and the blood pressure is low. The heart and the circulatory system are insufficiently filled with blood whereas the blood stores, especially in the portal venous area, are overstocked with stagnating blood. The patient is drained of blood from the stores. Clinically he is collapsed: the skin is pale and cold, the nose peaked, the brow damp, the pulse fluttering, the heart small, the veins of the skin almost empty of blood, the liver swollen, the urinary secretion scanty. Aetiologically two groups of collapse can be distinguished: the toxic and the reflex type. In the former the small vessels of the peripheral circulation are paralyzed by poisons of chiefly an amine character. In the latter, by irritation of nervous receptors a reflex disturbs the vasomotor system. Cases of toxic collapse are mostly of a protracted nature and often end fatally. The reflex cases

generally pass off more quickly and are seldom dangerous to life. In table 2 some examples are given from cases showing various types of collapse:—

TABLE 2.
CIRCULATING BLOOD VOLUME IN CASES OF COLLAPSE.

CASE NO.	AGE	WEIGHT KGM.	HAEMO-GLOBIN PER CENT.	RED CELL MILL. PER C.M.	ALBUMIN IN SERUM PER CENT. *	CELLS PER CENT.	PLASMA VOLUME C.C.	CELL VOLUME C.C.	BLOOD VOLUME		CAUSE OF THE COLLAPSE
									C.C.	PER CENT. BODY WEIGHT	
69	4 mths.	6.2	—	—	—	30.8	317	139	456	7.4	Intussusception and peritonitis
289	3 mths.	4.69	92	4.78	7.5	38.5	162	103	265	5.6	Alimentary intoxication.
—A		4.93	72	3.54	5.2	36.3	240	139	379	7.7	Recovered ten days later
291	8½ yrs.	22.5	90	4.80	8.9	48.4	721	677	1398	6.2	Toxic diphtheria in seventh week. Myocarditis with protracted collapse.
—A		22.9	82	—	7.9	46.5	696	599	1295	5.7	Fourteen days later, still collapsed
—B		23.2	80	3.80	7.9	41.6	920	664	1584	6.8	Cured one month later
248	15½ yrs.	40.3	88	4.32	—	47.3	1801	1622	3423	8.5	Orthostatic child in lying position
—A		—	—	5.48	—	46.2	1355	1164	2519	6.3	After ten minutes standing, collapse, orthostatic albuminuria

* By refractometer.

Cases of toxic collapse often occur in children after wounds from accidents or operation, and also from severe burns. Both are caused by histamine-like poisons, which also bring about the fever. There are often other causes also mentioned later which disturb the circulation like collapse, e.g., after operations on intussusception, through the absorption of intestinal poisons into the blood, the simultaneous narcosis, reflex shock from the peritoneum, etc. An example of an infant with intussusception and peritonitis is to be seen in table 2. The circulating blood volume is only slightly diminished, but it must be remembered that the child had a high degree of fever and that fever as such increases the blood volume. The scientific basis for subcutaneous or intravenous infusions especially in the form of constant drip infusions for such cases is clearly demonstrated.

Much investigation has been carried out in the cause of toxic collapse in alimentary intoxication of infants. The clinical appearance is recog-

nizable at once. For some time the attention of certain paediatricians has been attracted by the slowing down and gradual disappearance of the first heart sound and the noticeable small heart shadows in the x-ray photograph. Both these factors have been explained by measuring the circulation volume in the case of toxic infants (see table 2). The circulating blood volume is much decreased and the blood thickens at the same time. As a consequence, the circulation time is greatly prolonged, the heart receives too little blood per time unit, contracts in proportion and propels its tiny output with weak systolic contractions. Besides the heart, the skin and the central nervous system also receive too little blood; vomiting and periods of unconsciousness are increased by anaemia of the brain. A great deal of the blood is stored in the depôts. In the example given, more than 100 c.c., i.e. about a quarter of the normal circulating blood volume of this child, is stored in this way. The depôts are chiefly the lungs and the portal venous area, as can be deduced from the state of the chest, the swelling of the liver and the inflation of the abdomen. The inadequate blood circulation in the intestines and liver encourages, in the manner of a vicious circle, the re-absorption of shock-producing poisons from the bowel into the blood causing the alimentary intoxication. Therapy has always taken this into account by giving subcutaneous or intravenous infusions, stimulants and hot baths.

The last big group of cases of toxic collapse is that in which collapse is caused by acute infectious diseases such as diphtheria, scarlet fever, dysentery and typhoid, as well as in the crisis of lobar pneumonia. In these cases, the circulatory disturbances which are not primarily caused by a failure of the heart have been the subject of original observations by the author. Admittedly, very often a combination of toxic collapse and heart failure due to myocarditis is found as in the example of post-diphtheritic circulatory disturbance in table 2. Two of three investigations were made here during the developing collapse. The circulating blood volume was in both examinations greatly diminished, in the first case with simultaneous thickening of the blood, in the second case after some hydraemia. This seems to indicate the first stage of recovery from collapse, for the same was observed in the case of an infant with alimentary intoxication. At the third investigation of the diphtheritic child during convalescence the circulating blood volume was 200 to 300 c.c. greater than during the collapse. Admittedly, it had not yet reached the normal figure. Opinion has traced circulatory disturbance of this kind back to a toxic paralysis of the vasomotor nerve centres. Yet tests on diphtheria-poisoned animals have proved that the vasomotor centres can be excited normally by reflex action even shortly before death and histologically they are intact in children dying from diphtheria. It must therefore be assumed that the diphtheria toxin and the other infectious poisons attack the peripheral circulation directly, and first the vessels of the liver and bowels. The treatment is the same as in the other forms of toxic collapse, but when myocarditis is present great care must be taken to avoid overloading the circulation and abruptly raising the blood pressure.

Reflex collapse can be brought about by irritation of the various nervous receptors. The irritation reaches the vasomotor centres and from here passes on to attack the vasodilators and constrictors always in the same way, the tone of both being changed, resulting in a dilatation of the vessels especially in the portal venous area. A reflex collapse can also be caused by excitement of the ordinary sensory nerves, that is to say by severe pain. This is probably what happens in the case of traumatic shock, leading often to fainting. It occurs also as a result of irritation of the peritoneum, e.g. a blow on the abdomen, laparotomy, etc., and in principle is represented by the Goltz tapping test.

The majority of the cases of reflex collapse are caused by irritation of the sensory nerves. For example, a feeling of nausea can be caused by an intolerable smell or taste, vomiting may begin and acute collapse can follow. The principal receptor for bringing on reflex collapse is the compensatory organ of the aural labyrinth. The distressing condition to which seasickness can soon reduce even a healthy and robust person is well known. Also the motion of a train, motor car and aeroplane can lead to similar reactions. Likewise the same effect is found in some children after riding on a roundabout, or on the swing.

The most frequent and important of the forms of statically-caused reflex collapse in childhood is a group which is considered under the general name of 'orthostatic vasoneurosis' or 'orthostatism.' Mostly these are cases of disproportionately-grown, apparently anaemic neuropathic children between the ages of five and fifteen, who in extreme cases have a seasick-feeling merely from standing up after lying down, or after standing for only a short time. The face becomes pale and damp, the pulse small and frequent, and yawning, nausea, vomiting, dark spots before the eyes and giddiness appear. Suddenly the child falls down in a faint. After a few minutes in a horizontal position recovery takes place. The examination of the circulation in this condition shows the classic type of collapse: the blood pressure is low, the arm veins are poorly filled, the circulating blood volume has decreased by 25 per cent. of what it was when lying (see table 2), the circulation time has lengthened, the heart is poorly supplied and small, the brain practically without blood. Several hundred c.c. of blood stagnate in the depôts especially in the sub-papillary plexus of the legs (the calves look livid), and in the abdomen. Admittedly, among these the kidneys need special mention. During the collapse while standing these organs—as also the heart and the brain—are insufficiently supplied with blood and react because of their sensitivity to lack of oxygen, within a short time presenting typical functional changes, namely, oliguria and albuminuria.

Thus an explanation can be offered for the much-discussed orthostatic albuminuria. The tracing of this from orthostatic circulation collapse and the consequent anaemia of the kidney is supported by the following results of the writer's researches:—

After one hour's diathermy of the kidney region, both in short-period attempts to stand as also in whole-day standing up, a strong and occasionally

complete suppression of the albumin secretion takes place as a result of attracting blood to the kidneys. The same observation has been made simultaneously by other writers. Orthostatic albuminuria is not necessarily a concomitant of orthostatic collapse, but is seldom absent in severe cases. In slight cases of orthostatic vasoneurosis—for not all cases are as severe as the one above described—the albumin secretion is often missed.

(c) **Pneumonia in early childhood.**

The fate of the infant or young child with pneumonia depends mainly less upon the local process in the lungs as on the reaction of the circulatory system to the pulmonary disturbance and the intoxication of the infective process. Attention must therefore particularly be paid to the condition of the heart and the peripheral circulation in cases of pneumonia among young children. The first question at the bedside of a pneumonic infant is 'Is the circulation compensated or de-compensated?' A convenient indicator is the colour of the child's skin. If the skin, especially in the face and at the extremities appears rosy, pale red, or even highly flushed, then there is a good reaction to the fever, pointing to compensation. Decompensation is present when a distinct cyanotic, blue, grey-blue, or pale grey hue is seen, or when a waxlike paleness is present, with only a faint hint of red or blue mixed in it. From the purely clinical point of view three types of pneumonia can be distinguished, the red, the blue and the pallid type. The state of the circulation in these three types has been investigated and an attempt made to relate this to the state of the lungs, the degree of dyspnoea and to the general state of the child. The writer's experience is limited to twelve children most of whom had whooping cough. The results of research into the state of the circulating blood volume in these three types will first be recorded.

TABLE 3.

CIRCULATING BLOOD-VOLUME IN INFANT PNEUMONIA.

1. RED TYPE (average of five experiments)	Circ. plasma 6.0 per cent. Circ. blood volume 9.2 per cent. of body weight.
2. BLUE TYPE (average of six experiments)	Circ. plasma 4.5 per cent. Circ. blood volume 7.3 per cent. of body weight.
3. PALLID TYPE (average of five experiments)	Circ. plasma 6.1 per cent. Circ. blood volume 10.0 per cent. of body weight.

1. **In the red type of pneumonia** in young children the circulating blood volume is found to be increased as compared with the average and individual normal levels. It is a typical fever reaction, which is found also in non-pneumonic infections. It is comparable with the febrile increase of the basal metabolism. Actual circulatory disturbances are not present. Dyspnoea is slight, the general state of health not greatly affected. The lung condition is generally localized, the course of the illness proceeds slowly, the prognosis is favourable.

2. **In the blue type of pneumonia** the circulating blood volume is reduced, which, in view of the fever, is specially noticeable. The sub-papillary plexus of the skin swallows up much blood, the skin cools as a result of slowness of blood, the liver is swollen, the abdomen distended, the

blood pressure is low, the pulse rate high, the heart dilated on the right side and the lungs engorged with blood. This is a so-called collapse-decompensation of the circulation. The dyspnoea is much more marked than in the 'red' cases, the muscles often atonic, listlessness is pronounced, with alternating apathy and restlessness. In the lungs is generally found a widespread pneumonia, accompanied by bronchiolitis. The course of the disease is swifter, the prognosis generally bad.

3. **The pallid type of infant pneumonia** is accompanied by an increase of the circulating blood volume. The pallid skin of the child does not feel cool, it is hardly cyanotic, the liver is not large, the abdomen not uniformly distended. Pulse and respiration rates are high, increasing during fits, and muscle tone is absent. An enormous quantity of blood is (with increasing speed?) pumped through; the retentive ability of the depôts seems nil, the heart is overburdened and gives out. Most of these pallid cases have the appearance of bronchiolitis with changing areas of pneumonia. The course of the illness is often very rapid, the prognosis very unfavourable.

In spite of the small number of the investigations they do appear to give indications for the general lines of treatment of the circulatory system in pneumonia among young children. The 'red' or compensated type of pneumonia naturally needs no such treatment. In the 'blue' type measures must be taken to increase the circulation blood volume and to empty the depôts, thereby relieving the right side of the heart.

The following can be recommended: (1) warm applications, hot baths, etc.; (2) stimulation by caffeine, camphor preparations, adrenaline, etc.; (3) small venesections, about 30 to 40 c.c. (repeatedly if necessary). Concentrated and bulky food must be avoided and the child must not sit up or be carried about unnecessarily.

In the 'pallid' type the following general indications can be recommended:—(1) Sedatives (chloral hydrate, codein, etc.); (2) digitalis or strophanthin; (3) large venesections, either bloodless in the skin (mustard bandage for a few minutes) or abstracting blood by puncture, venesection or arteriotomy (about 100 c.c.). The above-mentioned excitants and the overfilling of the bowel with liquids must be avoided. Care must be taken to provide plenty of fresh air treatment, routine sedatives and if necessary oxygen inhalation (ten minutes an hour) in all forms of pneumonia.

(d) Hyperthyroidism and Hypothyroidism.

In hyperthyroid children the circulating blood volume is generally increased. The circulation time of the blood volume is highly increased, so that the minute volume of the heart reaches high figures. The opposite is the case in hypothyroidism and children with excessive adipose tissue.

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THE ROLE OF MUSCLE IN OBESITY

BY

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AND

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It is generally assumed that the increased weight of obese children is due to an increase of fatty tissue. In the following paper it is proposed to bring forward evidence which is suggestive that such an assumption is unwarranted and that, on the contrary, in the obese child the active muscular tissue shares in no small degree in the production of the abnormal weight.

Schaffer^{1, 2} has pointed out that the creatinine output is a good means of estimating the state of muscular development, and it is by a comparison of the creatinine output of normal and obese children that an attempt has been made to determine in how far fat and muscle are responsible for the increased weight. Schaffer states that, assuming the muscles in an adult man to form 50 per cent. of his body weight, 50 mgm. creatinine on the average are formed by one kgm. of muscle in twenty-four hours. If this estimate is accepted, and there is no evidence that infantile or adolescent muscle is in this respect different from adult muscle, it is possible to determine from the total daily output of creatinine and the weight of the child what proportion of the body weight is due to active muscular tissue. It is known, however, that the proportion of muscular tissue varies with age (Rougichitch³) so that it is essential that in any comparative study during childhood only children of approximately the same age should be contrasted.

Material.

The obese children forming the objects of the present study comprise those who had been referred to hospital during the last two years on account of a too-rapidly increasing weight. In the selection of the controls for comparison with these obese children sex, height and weight was taken into consideration as well as age. Under normal conditions the proportion of fat and muscle is not the same in both boys and girls, hence children of the same sex only are compared. The height of the child also determines the amount of muscular tissue present, and it may be pointed out that in both the obese and control cases this varied within the narrow limits of 96 and 106 per cent. expected height for age. The weight of the control cases varied between 81 and 107 per cent. of the normal standard for the appropriate age. The control children appeared to be in good health at the time of the examination and for the most part were convalescent from such conditions as chorea and subacute rheumatism.

Methods.

The obese and the normal children studied were confined to bed in hospital and they were given a standard creatine-free diet during the whole course of the investigation. In this way the diet and the urinary output could be controlled. After two preliminary days, the total urine was collected and two successive twenty-four hours' specimens, i.e., those of the third and fourth days, were examined for the creatinine and creatine content according to the method of Folin.

Results.

Table 1 shows the average creatine output in twenty-four hours, the age, sex, actual weight, estimated amount of muscular tissue and the percentage of this to the body weight. The creatine nitrogen coefficient has been included in this table because it is the usual means of expressing the muscular state of the individual. It does not appear, however, that the creatinine coefficient is particularly suitable for the child, varying as this does with age because of the different proportion of muscle present as the child gets older. This rise of the coefficient from between 5 and 6 in the fifth year to between 7 and 8 in the fourteenth year is evident in the control cases. True, on the average the creatinine coefficient is lower in the obese children and does not show the same rise with age, but there is a considerable overlap, especially among the children under eleven years of age when there is really no difference between the normal and the obese, but what is more important, there would not seem to be any correlation between the coefficient and the degree of obesity as estimated by the relative percentage of increased weight for age.

The figures in table 1 indicate that the increase in body weight of the obese child is not due to fat alone, but that this increase concerns the active tissue as well. Age for age there is a consistent, excessive creatinine output in the obese patients and in some instances this would seem to represent a relatively greater increase in active tissue than would be expected from the increased weight. If, for example, case 2 of the obese group is compared with case 1 of the controls, it is seen that the total weight of the obese child is 158 per cent. of that of the control child, while the muscular tissue of the obese child, as estimated by the creatinine output, is increased to 170 per cent. of that of the control.

The relative increase in total weight and in active muscular tissue is well shown in table 2 where the findings in the obese child are expressed as the percentage of the findings obtained in the case of a control child of the same age and sex.

In every case there is evidence of an increased amount of muscle tissue, in two instances the percentage increase in muscle is in excess of that of the total weight, in four instances the percentage increase in muscle and

THE ROLE OF MUSCLE IN OBESITY

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TABLE 1.

CASE NO.	SEX.	AGE IN YEARS.	WEIGHT KGM.	PERCENTAGE OF EXPECTED WEIGHT.	CREATININE EXCRETION MGM.	CORRESPONDING TO MUSCULAR TISSUE KGM.	PERCENTAGE OF ACTUAL BODY WEIGHT.	CREATININE COEFFICIENT.
NORMAL CHILDREN.								
1	m.	5 $\frac{1}{2}$	17.2	92	271	5.42	31.5	5.9
2	m.	5 $\frac{1}{2}$	17.1	91	254	5.08	29.7	5.5
3	f.	8 $\frac{6}{12}$	21.1	84.4	350	7	33.2	6.2
4	f.	7	22.6	104	438	8.76	38.7	7.2
5	m.	7 $\frac{9}{12}$	25	101	459	9.18	36.7	6.8
6	f.	9 $\frac{1}{12}$	25.5	81	444	8.88	34.8	6.5
7	f.	11 $\frac{1}{12}$	33.6	95	722	14.44	42.9	8.0
8	f.	11 $\frac{1}{12}$	32.7	89	645	12.9	39.4	7.3
9	f.	12	37.7	102	715	14.3	38.4	7.0
10	f.	12 $\frac{6}{12}$	41.2	107	646	12.9	31.3	5.8
11	f.	12 $\frac{7}{12}$	37.7	95	817	16.34	43.3	8.1
12	f.	12 $\frac{9}{12}$	33.9	83	625	12.5	36.9	7.4
13	m.	12 $\frac{9}{12}$	35.7	89	655	13.1	36.7	6.8
14	f.	13	38.2	85	778	15.56	40.7	7.6
15	f.	13 $\frac{5}{12}$	39.5	89	726	14.52	39.3	6.8
16	f.	13 $\frac{10}{12}$	38.2	91	790	15.8	41.5	7.7
OBESE CHILDREN.								
1	m.	4 $\frac{1}{12}$	30.4	170	365	7.3	20	4.4
2	f.	5 $\frac{2}{12}$	27.3	150	436	9.26	33.9	5.9
3	m.	8 $\frac{5}{12}$	34.5	121	653	13.06	37.8	7.0
4	f.	9	43.2	170	717	14.34	33.2	6.2
5	f.	12 $\frac{2}{12}$	64	169	927	18.54	29	5.4
6	f.	12 $\frac{6}{12}$	65	165	1,006	20.12	30.9	5.9
7	f.	12 $\frac{6}{12}$	51.4	131	816	16.32	31.7	5.8
8	f.	12 $\frac{6}{12}$	51	129	831	16.62	32.6	6.1
9	f.	12 $\frac{7}{12}$	73.1	187	923	18.46	25.3	4.7
10	f.	12 $\frac{10}{12}$	64.8	154	951	19.02	29.3	5.4
11	f.	12 $\frac{10}{12}$	77	190	1,253	25.06	32.5	6.1
12	f.	13	77	173	1,252	25.04	32.5	6.1
13	f.	13 $\frac{9}{12}$	77	169	1,231	24.62	31.9	6.0
14	f.	13 $\frac{9}{12}$	55.9	131	925	18.5	33	6.2

in body weight are practically identical and in six the percentage increase in body weight is in excess of that of the muscle. Yet in all but three of the latter, the difference between the increase in total weight and in muscle does not exceed 30 per cent. In only one case, no. 9 of the obese group, is this difference really great. This child suffered from an old septic

TABLE 2.

CASE NO.	OBESE OR NORMAL.	WEIGHT KG.M.	OVERWEIGHT OF OBESE OVER NORMAL CHILDREN PER CENT.	ACTIVE MUSCULAR TISSUE KG.M.	OVERWEIGHT OF MUSCULAR TISSUE OF OBESE OVER THAT OF NORMAL CHILDREN PER CENT.	CREATININE COEFFICIENT
2 1	ob. n.	27.3 17.2	158	9.26 5.42	170	5.9 5.9
3 3	ob. n.	34.5 21.1		13.06 7.00		7 6.2
4 6	ob. n.	43.2 25.5	169	14.34 8.88	162	6.2 6.5
5 9	ob. n.	64 37.7		18.54 14.3		5.4 7.0
6 10	ob. n.	65 41.2	160	20.12 12.9	157	5.9 5.8
7 10	ob. n.	51.4 41.2		16.32 12.9		5.8 5.8
8 10	ob. n.	51 41.2	123	16.62 12.9	128	6.1 5.8
9 11	ob. n.	73.1 37.7		18.46 16.34		4.7 8.1
10 11	ob. n.	64.8 33.9	191	19.02 12.5	152	5.4 7.4
11 13	ob. n.	77 35.7		25.04 13.1		6.1 6.8
12 14	ob. n.	77 38.2	201	25.04 15.56	161	6.1 7.6
13 15	ob. n.	77 39.5		24.62 14.52		6.0 6.8
14 16	ob. n.	55.9 38.2	146	18.5 15.8	117	6.2 7.7

arthritis of the right hip joint with ankylosis and atrophy of the right leg and an underdevelopment of the muscles of the left leg; case no. 11 of the control series, with whom she is compared, was a particularly muscular child with the highest creatinine output of the normal series. Nevertheless the child showed an increase of muscular tissue of 13 per cent. compared with a well-developed control. The relation between the increase in muscle

and increase in weight is shown graphically in the accompanying chart and reveals in a striking fashion the parallelism which exists between them.

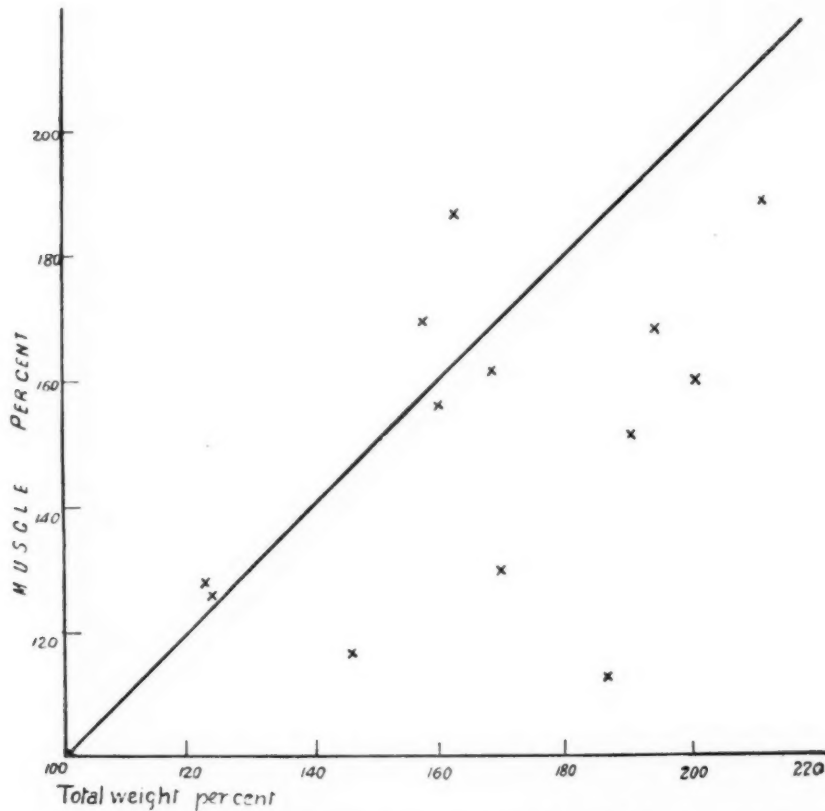


CHART.—Showing relation between the body weight and muscle weight in the obese children. On the ordinate are given the body weight and on the abscissa the muscle weight as percentage of normal. The chart shows the findings from table 2 graphically.

Creatine-creatinine tolerance.

It might of course be argued that the creatine-creatinine metabolism is modified in the obese state and hence comparisons such as the above are unjustified. To explore this possibility a suggestion made by Prof. Andrew Hunter was adopted to test the tolerance of both types of children against ingested creatine and creatinine. This was carried out in the following manner.

After the children had been kept on a creatine-free diet and their average basal excretion of creatinine and creatine established, they were given in the first place 500 mgm. of creatinine by mouth, the urine being collected during three successive days and the excess of creatinine over the basal amount determined. When the basal conditions were once more reached the children were given 500 mgm. of creatine, the urine again collected on the following three days and the output of creatinine and creatine ascertained. Details of the findings are given in table 3.

TABLE 3.—CREATININE AND CREATINE TOLERANCE.

CASE No.	SEX.	AGE IN YEARS.	WEIGHT KGM.	PER-CENTAGE OF EXPECTED WEIGHT.	CREATININE SURPLUS AFTER CREATININE INGESTION. MGM.	PER-CENTAGE OF AMOUNT INGESTED.	NORMAL LEVEL REACHED IN DAYS.	CREATININE CO-EFFICIENT.	CREATINE SURPLUS AFTER CREATINE INGESTION. MGM.	NORMAL LEVEL REACHED IN DAYS.	CREATININE SURPLUS DUE TO CONVERSION. MGM.	NORMAL LEVEL REACHED IN DAYS.	TOTAL SURPLUS. MGM.	PERCENTAGE OF CREATINE INGESTED PER CENT.
1	f.	7	22.6	104	412	82	2	7.2	283	2	16	1	299	60
2	m.	7 $\frac{1}{2}$	25	101	498	99	2	6.8	268	2	21	2	289	58
3	f.	11 $\frac{1}{2}$	33.6	95	478	95	1	8.0	111	1	221	1	332	66
4	f.	12	44.5	120*	510	102	2	6.7	233	1	64	2	297	59
5	f.	12 $\frac{6}{12}$	41.2	107	508	102	2	5.8	179	2	287	3	466	93
6	f.	12 $\frac{7}{12}$	37.7	95	486	97	2	8.1	264	3	253	3	517	103
7	f.	12 $\frac{1}{12}$	33.9	83	467	93	3	7.4	231	1	65	2	296	59
8	f.	13	38.2	85	497	99	2	7.6	201	1	214	2	415	83
9	f.	13 $\frac{10}{12}$	38.2	76	520	104	1	7.7	155	1	185	2	340	68
10	m.	4 $\frac{8}{12}$	30.4	171	466	93	2	4.4	312	3	132	3	444	89
11	f.	5 $\frac{3}{12}$	27.3	150	412	82	1	5.9	275	2	174	3	449	90
12	m.	8 $\frac{6}{12}$	34.5	121	483	97	1	7.0	176	2	194	3	370	74
13	f.	12 $\frac{5}{12}$	64	169	433	87	1	5.4	281	3	58	2	339	68
14	f.	12 $\frac{6}{12}$	65	165	542	108	3	5.9	362	3	102	4	464	93
15	f.	12 $\frac{6}{12}$	51.4	131	471	94	2	5.8	238	1	223	3	461	92
16	f.	12 $\frac{7}{12}$	73.1	187	498	100	1	4.7	215	1	79	2	294	59
17	f.	12 $\frac{11}{12}$	64.7	154	518	104	1	5.4	169	1	218	2	387	77
18	f.	13 $\frac{6}{12}$	55.9	131	518	104	1	6.2	138	1	111	2	249	50

* This child was very tall and had the appearance of a perfectly normal girl of about 13 $\frac{1}{2}$ years.

From the above findings it would appear that there is no tolerance of either the obese or normal child to creatinine. Only three of the eighteen children (obese and normal combined) excreted less than 90 per cent. of the ingested creatinine, and in these particular cases the poor excretion may be attributed to defective absorption. Eight of the children had excreted the ingested creatinine within twenty-four hours, eight reached the normal level within forty-eight hours, and in the remaining two (one normal and one obese) the surplus excretion continued for three days.

In the case of the ingested creatine, on the other hand, the excretion was more complex. First of all there resulted an immediate increase in the basal output of creatine. The total amount excreted varied within wide limits, but it did not seem to be influenced by sex, age or the weight of the child. At the same time, or on the following day, the creatinine excretion also rose above the average basal level, due apparently to a conversion of some of the creatine into creatinine. The amount thus converted also varied within wide limits and, similarly, did not seem to have any relationship to the sex, age or weight of the child.

These findings do not reveal any difference in the creatine-creatinine tolerance nor in the creatine-creatinine metabolism of the obese and normal child, and hence the comparison of the creatinine output of children of the same age would seem to be justified.

Conclusions.

1. The creatinine and creatine metabolism is the same in the obese and in the normal child.
2. There is no tolerance of the normal or obese child for creatinine, fully 90 per cent. of the amount ingested by the mouth being excreted in the urine.
3. The daily output of creatinine of the obese child is invariably above that of the normal child of the same age.
4. In the majority of examples of obesity studied (7 out of 13) the percentage increase of creatinine excretion is commensurate with the percentage increase of the weight of the child.
5. In the so-called obese child the increase in weight is as a rule due as much to increase of muscle as to increase of fat.

We wish to express our gratitude to Dr. Leonard Findlay for his suggestions and his kind help.

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A CONTRIBUTION TO THE PATHOLOGY OF IDENTICAL TWINS

BY

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It must first be stated that the diagnosis of the type of twinning in each of the cases here described was made by a midwife, the women being delivered at their own homes and not in hospital. There is still controversy about the best method of diagnosis and Reichle¹ is of opinion that even reports of membrane examination are valueless unless they describe the condition of the septum. In monochorionic twins the septum should be composed of amnion only. It was not possible in the present cases to gain any information about the septa, but all three midwives have been certain that there was only one placenta and one chorion. It is well known that Siemens's method² is unreliable when applied to infants and young children in as much as congenitally determined characteristics may have a delayed manifestation; this especially holds true for the colour of the iris.

I myself am fully convinced that these three sets of twins are really monozygotic, their similarity being so striking.

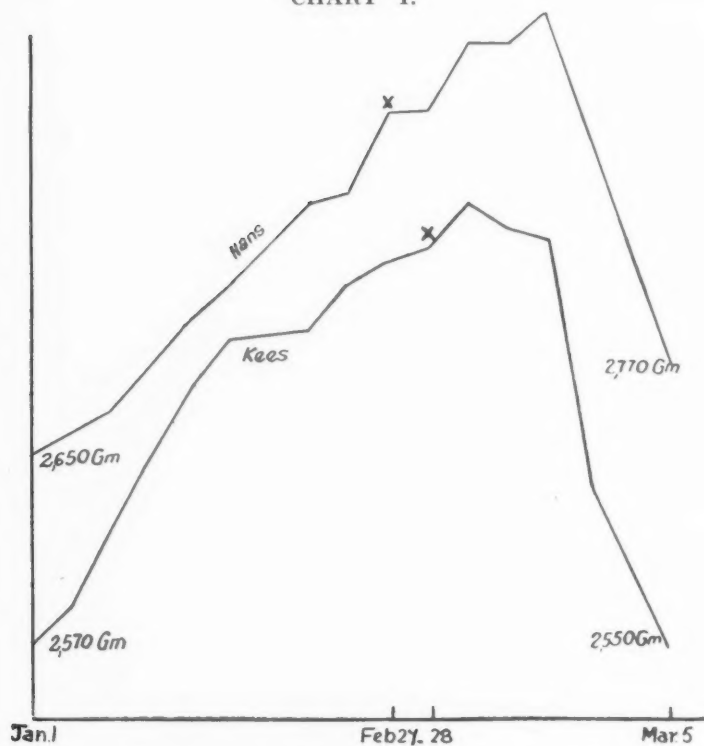
Case record—first pair.

C. F., born 22.7.1921, was sent to the Hospital for Sick Children in Amsterdam on account of pyloric stenosis and was there under my care from October 22 till December 24, 1921. The child received medical treatment, left almost cured and developed in a normal way. Afterwards she became maternal aunt to the twins H and K. These children, boys, were born on January 30, 1935, six weeks before term. H was born as a breech presentation, weighing 2,570 gm. He was not asphyxiated. K weighed 2,650 gm. and was slightly asphyxiated but soon developed a normal colour. Both children were breast fed and at first all went well, the children steadily increasing in weight. On February 26 projectile vomiting abruptly set in with H. The weight continued to increase with two interruptions till March 3, when a considerable drop was noted. K began forcible vomiting on February 27. At first he continued to gain weight but later there was a slow and then a rapid fall in weight. The children were admitted to the clinic on the evening of March 4 and on the following morning the weight of H was 2,770 gm. (length 47 cm.) and that of K 2,550 gm. (length 49 cm.) (fig. 1).

As medical treatment was of no avail Rammstedt's operation was performed in both cases by the late Professor O. Lanz on March 11, the weight of H being then 2,610, that of K 2,490 gm. Both children presented the typical olive-shaped pyloric tumour,

that of K being somewhat larger than that of H. The immediate effect of the operation on the general condition was quite remarkable. The children who before had been ill at ease, fretful and drowsy with a tense facial expression, went peacefully and happily to sleep and awoke in an altered condition. The evening temperature of H was normal; in K there was a slight rise*.

CHART I.



× Projectile vomiting sets in.

The course in K ran quite uneventfully. The mother came to the clinic to feed her children and as a supplementary food, buttermilk with flour and sugar was given after the well-known formula. On leaving the clinic on April 10 K weighed 3,700 gm.

With H there was some trouble; he developed diarrhoea and only progressed slowly, but after some time all went well and he left hospital on the same day as his brother, weighing 3,710 gm. their weights being now practically equal.

Similar cases.

Pyloric stenosis as a concordant symptom in monozygotic twins has been observed by Varden³ (boys; vomiting setting in a month after birth, no peristaltic waves but typical pyloric tumour found on operation.) The same

* According to L. F. Meyer and E. Nassau (*Die Säuglingsernährung*, 1930) there is almost always a fever of unknown origin in the evening after the Rammstedt operation. In my own experience this fever is often absent.

author had a personal communication from Moore and Bilderback¹ that their cases also occurred in monozygotic twin boys. Sommer's observation² is interesting, as the monozygotic twins were girls. In one the vomiting set in on the twelfth day after birth, in the other one on the eleventh.

From the point of view of heredity the fact that the maternal aunt also suffered from the same illness adds special interest to the present observation.

In the fourth of his interesting experiments on identical twins with unboiled and boiled breast-milk respectively, Bernheim-Karrer⁶ mentions without further details that both children had forcible vomiting (not real pyloric stenosis as he emphatically states), but with one of the twins the vomiting was much less than with the other. This marked difference in identical twins is noteworthy, but, as the author says himself, it might be possible that the boiling of the milk in causing a thickening of the fluid, had worked as a therapeutic measure. Lasch⁷ reports the following case:—

Diagnosis of monozygotic twinning was made in the Obstetrical Clinic of the University of Breslau on account of monochoria. There was also a striking similarity of pigments of iris and hair and of the shape of the head. At the end of the third week in one of the children, who were both breast fed, the symptomatology of pyloric stenosis set in. Operation was considered, but an influenzal infection proved fatal. Post-mortem examination confirmed the diagnosis. The other twin never presented symptoms of pyloric stenosis.

Bernheim-Karrer in discussing this case is not wholly disinclined to doubt the identity of the twins. However, Lasch does not leave much room for doubt, but expresses himself guardedly as to the conclusion to which his observation entitles him. Before stating that heredity plays no part and that parakinetic factors are responsible, he claims the necessity of a larger number of observations, as in exceptional cases an unequal distribution of factors during cleavage may take place, or an 'idiokinesis' in utero or a marked variability of the heredity factors ('Erbanlage') may be present.

Discussion.

Before they were operated upon and also when they were five-and-a-half months old I studied these twins. It is well known that in so-called congenital pyloric stenosis the symptoms do not begin at birth, but only after a lapse of time. In the records of our clinic the longest duration was five weeks, but in the medical literature still longer periods are mentioned. All authors agree that it is not the stenosis but the supervening spasm which causes the peristalsis and the forcible vomiting. It is therefore pertinent to ask what is the underlying cause of the spasm? Some attribute it to a nutritional disorder of the child, others to a defect in general care, but in the present instance the children were well fed and well cared for. They showed not a single intestinal or other trouble before the spasm set in. Another cause, probably intrinsic must be looked for and it is tempting to think of the hormonal influences. Having hitherto kept one another in balance,

one now begins to predominate. The second step is to presume the dominant hormones originate from the mother's milk or the mother's placenta. The hereditary factor then shows itself in the fact that the twins' grandmother, has produced a hormonal spasm in the pylorus of her other daughter, the maternal aunt to the twins. Although this is a speculative hypothesis, it is clear that no extrinsic influence can be made responsible for the beginning of the spasm in both children almost on the same day.

Boys (80-85 per cent.) are much more frequently affected than girls; this fact has lead Stolte⁸ to the hypothesis that the hormones which in pregnancy establish the growth of the uterus of the mother, after being transmitted by the placenta or by the milk of the mother to the child, are responsible in newborn girls for the relatively large size of the uterus and in newborn boys they affect another muscular organ, the pylorus. Children with pyloric stenosis (spasm) almost always have nervous, 'neuropathic' parents and themselves often exhibit other symptoms of neuropathy.

That the hypertrophy of the pylorus is secondary to 'overwork' ('Arbeitshypertrophie') brought about during intra-uterine life by a developmental neurosis seems highly probable. The paternal element in its origin can then also come in. I once saw a family where five children were affected with pyloric stenosis and several cases are mentioned in literature where more than one child suffered from it in the same family. In one of Feer's observations two children in one family had pyloric stenosis and it was proved that a child in another family who also was affected, had the same great-grandfather as those two children. Tj. Halbertsma⁹, of Haarlem, has recently given an interesting pedigree concerning the heredity of the disease.

H and K while staying in the clinic presented a striking similarity, but yet showed some differences. K had a pale naevus on the neck and one on the glabella; H had one on the neck only. Pale naevi in those places are almost of normal occurrence and have a tendency to disappear. So it is possible that the one on the glabella of H had already disappeared. There was some difference in the shape of the ears in each child. The right ear of H and the left of K having part of the border unfolded and the left ear of H and the right of K showing a broad lobule. This mirror-image effect is characteristic of monozygotic twins, but is not necessarily present. The feet of K had the plantar lines called by Brushfield¹⁰ 'A' (oblique plantar line), 'B' (transverse plantar line) and 'C' (transverse hallucial line). The left foot of H also showed these lines, but his right foot showed a deep oblique plantar line running to the mesial footborder, the transverse hallucial line not being clearly marked. An interesting fact is that K presented some symptoms of the exudative diathesis in the form of small papules in the face and that his stools were often greenish with small white particles, not amounting to diarrhoea and with steadily increasing weight. This was quite different from the frequent stools of H during part of his stay in hospital.

The children were re-examined at the age of five-and-a-half months. Their progress had been quite satisfactory (fig. 1). Leaving the hospital with practically the same weight. H, who had been heavier at birth, was now left behind. A month after their discharge H weighed 4,500 gm., K 5,050 gm.; from then onwards their weight curves run almost parallel, as is seen in chart 2.

K.

H.



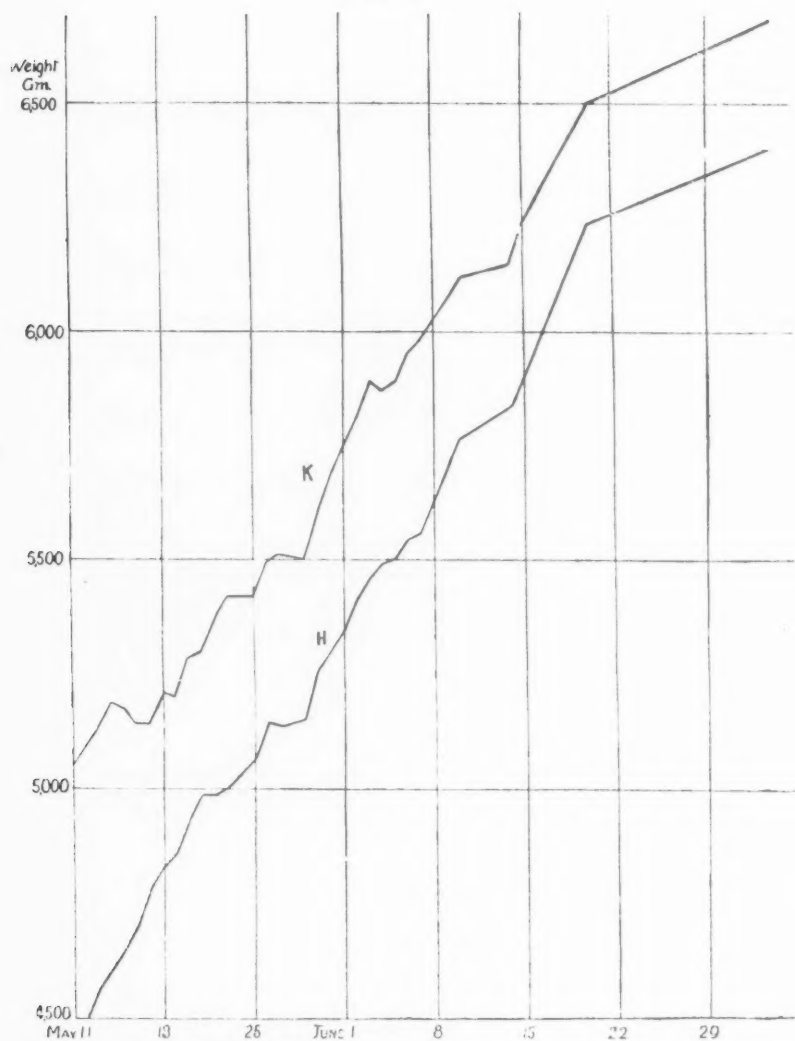
FIG. 1.—Both twins showing operation scars.
Age 5½ months.

SUMMARY OF EXAMINATION AT THE AGE OF FIVE-AND-A-HALF MONTHS.

					H	K
WEIGHT	6,800 GM.	7,200
LENGTH	65 CM.	66 CM.
LARGEST CIRCUMFERENCE	43 CM.	43 CM.
OF THE HEAD		
ANTERIOR FONTANELLE	2 × 2 CM.	2 × 2 CM.
CRANIOTABES	SOFT SPOT IN THE LEFT PARIETAL BONE NEAR THE LAMBOIDAL SUTURE	THE SAME
ROSARY	POSITIVE	POSITIVE
ABDOMEN	DISTENDED	DISTENDED
LIVER	NORMAL	NORMAL
SPLEEN	ENLARGED	ENLARGED
DESCENT OF TESTICLES	POSITIVE	POSITIVE
PALE NAEVI	NECK	NECK + GLABELLA

Both children appeared to be of normal intelligence. Their digestion was good; they did not show symptoms of the exudative diathesis. Their development appeared approximately normal. They were of a friendly disposition, laughing readily, but they were nervous and started at every sound. It is interesting to note that H loathed stewed apples and K had a preference for this fruit.

CHART II.



It will be seen from the summary of this examination that the children are in good health, but have developed rickets in exactly the same way. They were premature infants and rickets is widespread in Amsterdam. The fact that H did not develop any more symptoms of the exudative diathesis is interesting as also that they were still lacking in K.

That identical twins may show small differences in their somatic habitus, without the diagnosis of monozygotic twinning having to be rejected, is generally agreed upon.

Orgler¹¹ established discordancy in nine out of fourteen identical pairs of twins. This large number may perhaps be explained, says the author, by the fact that young infants are in the most labile period of the whole of human life and that the heritage ('Erbgut') may be altered by external stimuli, which afterwards will have no appreciable effect. It is well known that in identical twins the similarity increases as the persons grow older (see for instance the portraits in the article of Weitz mentioned below), whilst in dizygotic twins the likeness becomes less. In three of the pairs of twins which came under Orgler's observation the exudative diathesis ran quite different courses in one of the twins from that in the other one.

Case record—second pair.

The child F, boy, born November 11, 1934, was brought to the Clinic on April 13, 1935, for a right-sided, strangulated inguinal (scrotal) hernia. Both this child and his identical twin-brother, also called F, had within the first month of their lives developed bilateral scrotal hernias. In general the four hernias were unreduced as is shown in fig. 2, the children being quite happy in this state



FIG. 2.—Twins F., age 5½ months. Bilateral scrotal hernia in both twins.

according to the mother. In one of the boys the right half of the scrotum had become tender, swollen and of a bluish hue. The hernia then proved irreducible. In the Clinic the child was placed in his cot in a Trendelenburg position and an icebag applied to the swelling. In the course of a few hours the intestine could be returned to the abdominal cavity. Later the child was operated upon.

Some authors are of opinion that the cause of hernia lies for the greater part in extrinsic conditions. Siemens in his 'Zwillingspathologie' mentions 'M3 + ϕ ' (i.e. in three monozygotic twin pairs only one child had the

hernia, the other being free from it). Versluys¹² put it as 'M2 + ϕ ,' but Weitz¹³ found unilateral inguinal hernia 'M2 + +' and umbilical hernia 'M1 + +.'

In recent years more facts have come to light and Luxenburger¹⁴, who sums up the material, says: 'The heredity of the syndrome of feebleness of the connective tissue, which manifests itself amongst others in the tendency to pes cavus and pes planus and to hernia and constitutes a real stigma of the asthenic type of bodybuild, has been corroborated by the study of twins.'

In the literature I could find only one observation of bilateral hernia in identical twins (Hanrart quoted by Siemens) but as the original publication could not be consulted, further particulars cannot be given. As far as I know an observation of bilateral inguinal hernia developing so soon after birth, has not previously been published. Stransky¹⁵ records the following most interesting case history:—

Identical twins, boys, birth weight about 1,000 gm. were admitted to the hospital, aged two-and-a-half months. Their weight then was about 3,000 gm. Both had open inguinal rings but no hernia. On the fifth day after their admission both children went into convulsions of unknown origin, both developed a strangulated hernia and died after a few hours. At a post-mortem examination it was found in one twin that at the extreme end of the ileum a Littré hernia, about the size of the terminal phalanx of a finger, was strangulated in the left much enlarged, inguinal canal. Swelling and haemorrhagic infarction of testicle and epididymis was present together with thrombosis of the pampiniform plexus. In the other twin an open inguinal canal was present on the right side with haemorrhagic infarction of right testicle and epididymis and thrombosis of the pampiniform plexus.

Case record—third pair.

The child W born on July 17, 1934, was transferred to the Clinic on March 11, 1935, from one of the surgical wards, where she had been admitted on account of an acute glandular swelling at the angle of the jaw. W is the second of twin-girls. Both children were full-time babies, born spontaneously as head presentations. They were not asphyxiated. The weight of W was about 2,500 gm. and of her sister E about 3,500 gm. They were breast fed during the first month, then had buttermilk, after that milk and water with flour and sugar, and then mixed diet.

The twins are strikingly alike, according to the mother. Both had the rare combination of dark eyes and blonde hair (fig. 3). Even at birth W had already a natiform skull. On admission her weight was 6,730 gm. (at eight months), length 66 cm. There was only a mild degree of rickets present according to the x-ray pictures and blood-chemistry (Ca 11.2 mgm. per cent., P 4.9 mgm. per cent.). The largest circumference of the head was 46 cm., biparietal dimension 25 cm. There was a high forehead with marked bossing of the frontal eminences and somewhat less of the parietal ones. One small soft spot in the occiput was felt. The anterior fontanelle measured 7 × 6 cm., and was bulging with firm borders. Teeth were absent. There was no rosary and no

enlargement of the epipyses. The liver was not enlarged, the spleen was palpable, and there was slight divarication of the abdominal rectus muscles. Lumbar puncture showed pressure 32 cm., normal fluid, including microscopic examination. The Wassermann and Sachs-Georgi reactions in the blood were negative. After the lumbar puncture the tension of the anterior fontanelle has somewhat lessened.

During the child's stay in the hospital the mother was asked to bring the other twin for inspection. The clinical picture was the same. Rickets was present to a mild degree. The natiform

E. W.



FIG. 3.—Twins W. and E., age 8 months.

shape of the head was also present, but less pronounced, so that it could be readily understood why the mother spoke of the peculiar head of W and not of E. The largest circumference of the latter's head was 45 cm., the biparietal dimension 25 cm. The anterior fontanelle measured 7×6 cm., and also showed increased tension. A lumbar puncture was not feasible in the circumstances.

What is the underlying cause for the shape of the head and the increased pressure of the cerebrospinal fluid in these twins? Rickets, syphilis and prematurity may be left aside, the first because the natiform skull was already present at birth. Hydrocephalus generally produces a different shape to the head, yet the symptoms of the children can only be interpreted as caused by hydrocephalus. I believe that they have hydrocephalus, but the congenital anomaly which gives rise to the obstruction in the circulation of the fluid must of necessity be of little importance, otherwise the size of their heads would have been much larger. Perhaps already a fluid-balance has been established. It cannot be decided finally whether the shape of

head is dependent on the hydrocephalus or is an anomaly in itself. The fact that the natiform skull was more marked in W than in E can perhaps be explained by the influence of factors during intra-uterine life or during delivery.

Summary.

The study of identical twins has proved to be of the utmost value in separating the influences of heredity from those of environment. If clinicians make it a rule to observe and carefully follow up monozygotic and the dizygotic twins in their practice, they may render valuable services to science.

Three observations are here reported. The first describes pyloric stenosis in monozygotic twins and in their maternal aunt. The second shows inherited weakness of the connective tissue by the almost simultaneous appearance of bilateral inguinal hernias in identical twins. The third deals with mono-ovular twins, both with a natiform skull without any relation to prematurity, syphilis or rickets and also with a mild degree of hydrocephalus.

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FURTHER OBSERVATIONS ON PINK DISEASE

BY

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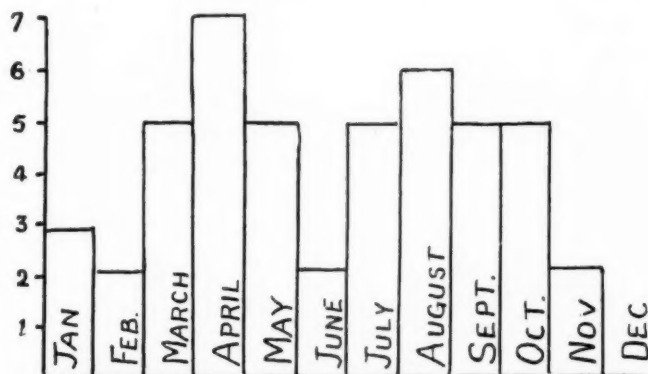
In a previous communication¹ the suggestion was made that pink disease is an abnormal reaction to daylight in an infected child. The chief evidence given in favour of this was as follows:—

The condition usually occurs after an acute infection of the respiratory tract; there is a marked seasonal incidence in the spring and summer (in this country) only four out of twenty-seven cases being admitted during the winter; twenty of the twenty-seven patients came from the country or suburbs; the disease was first described in Australia, and is prevalent in sunny countries; and, finally, protecting the children from daylight by keeping them in a room with windows of ruby glass caused a rapid improvement in their condition.

Further experience has confirmed this view. In 1933 and 1934 a further twenty-two patients suffering from this complaint were admitted to the Leicester Children's Hospital, making a total of forty-nine cases from the district since 1923. Of these forty-nine patients only eight were admitted between the months of November and February inclusive, while forty-one were admitted in the period from March to October. It is thus seen that the disease is one occurring in the time of long days and short nights, while during the coldest and darkest days it almost dies out. At the height of summer, however, the curve falls slightly, the greatest incidence being in April and August.

CHART I.

SEASONAL INCIDENCE.



The seasonal incidence, therefore, supports the hypothesis that the disease is in some way related to daylight. The ultra-violet rays, the rays of the visible spectrum, or the heat rays could conceivably be responsible. In this connection it is interesting to note that among the patients admitted in 1933, in which the summer was unusually hot, the death rate was high. Of ten patients admitted six died, and this was in spite of their being placed in a red windowed room, a manoeuvre which had previously apparently been successful. The case of one of these patients in particular is instructive and tragic.

He was a boy of nine months, and was admitted in May. At the time of his admission the 'red room' was occupied, and he was kept in the ward until it should be empty. On the morning of the second day the sun came round to the window above his cot, and owing to the time being that when the night and day staff changed over, this was unnoticed for half an hour. The child became very ill with a high temperature and a raised pulse and respiration rate and died the same evening.

It will be remembered that in the previous paper already referred to a patient with pink disease was deliberately placed in the sunlight and showed toxic symptoms within an hour, but recovered on being taken back indoors.

The effect of sunlight on blood.

In 1917 Clare², investigating the toxic effects of destroyed red blood cells, found that sunlight rapidly destroyed washed red corpuscles suspended in normal saline. Moreover he found that these destroyed cells possessed toxic properties when injected subcutaneously. This work was done in India, and in view of the association of pink disease with hot and sunny weather it was decided to perform similar experiments in this country. Blood from various individuals was collected with aseptic precautions from a finger prick in amounts of 0.1 c.c. and was suspended in 2 c.c. normal saline (pH 7-8) in test tubes of about 5 c.c. capacity. The blood was mixed with the saline by placing a finger covered with a sterile rubber finger stall on the open end of the tube and inverting. (Test cultures from these tubes proved that they were sterile.) The tube was then plugged with sterile cotton wool and was placed in the direct sunlight for three hours. It was then kept in the dark until the following morning (about eighteen hours) and readings for haemolysis were taken.

Blood was taken from thirty-one children between the ages of four months and nine years, suffering from various complaints, including four cases of pink disease, from three normal adults, and from four adult patients. It was found that in thirty out of thirty-eight cases complete haemolysis had occurred. The eight specimens which showed no haemolysis were all from patients with some form of anaemia. The blood from the normal adults haemolyzed as readily as the others, while that from the patients with pink disease showed no difference from the rest either in the rapidity or the extent of the haemolysis.

This destructive action of sunlight might be due to any of the three factors mentioned above—the rays of the ultra-violet end of the solar

spectrum, some of which may pass through glass and are known to be haemolytic; the rays of the visible spectrum; or the heat rays from the infra-red portion. It was decided to submit specimens of blood to the influence of each of these to determine which was the haemolyzing agent.

The effect of irradiating blood in vitro by ultra-violet light was investigated by Mr. C. J. Bond. Suspensions of 0.1 c.c. of blood in 2 c.c. of normal saline were used. Two suspensions were made in glass tubes similar to those used in the previous experiment, and two were made in quartz tubes of similar size. All four tubes were then subjected to irradiation from a mercury-vapour lamp. Complete haemolysis occurred in the quartz tubes, but none in the glass tubes. From this it was concluded that although ultra-violet light is a powerful haemolytic agent, the haemolysis obtained by exposing blood in glass tubes to sunlight was not due to this part of the solar spectrum.

The effect of white light on blood was investigated by adapting a microphotographic apparatus. An aluminium plate with a slit in it was placed in front of a two kilowatt lamp, and the rays coming through the slit were concentrated by means of a powerful convex lens, mounted on the optical bench, on to the glass tubes containing the blood suspended in saline. Three specimens of blood from normal adults and two from patients with pink disease were thus irradiated for six hours each. In no case was any haemolysis produced.

The effect of heat as a haemolytic agent is well known. To complete this investigation, however, suspensions of blood in saline were immersed in water baths at temperatures of 40° C., 52° C., and 55° C. Three specimens, one from a normal adult, one from a child convalescent from pneumonia, and one from a patient with pink disease, were immersed in the water bath at 40° C. for three hours, but no haemolysis occurred. Seven specimens (three from patients with pink disease) were immersed at a temperature of 52° C. Haemolysis occurred in all cases in time varying from one-and-a-half to three hours. Five specimens (two from patients with pink disease) were immersed at a temperature of 55° C. All showed haemolysis, four of them being haemolyzed in one-and-a-half hours, and one from a normal adult in two hours.

It appears therefore that the haemolysis produced by exposing blood suspended in saline in vitro to direct sunlight is due to the effect of heat.

Skin sensitivity to blood haemolyzed by heat.

The above results, taken in conjunction with Clare's work already referred to, suggested the possibility that pink disease is of the nature of an allergic reaction to heated blood. Intradermal injection of heated blood, however, failed to confirm this: 0.1 c.c. of citrated blood, haemolyzed by heat, was injected intradermally into the forearm of a patient with pink disease, and a similar amount of unheated citrated blood was injected into the skin of the other forearm. In fifteen minutes a small urticarial wheal

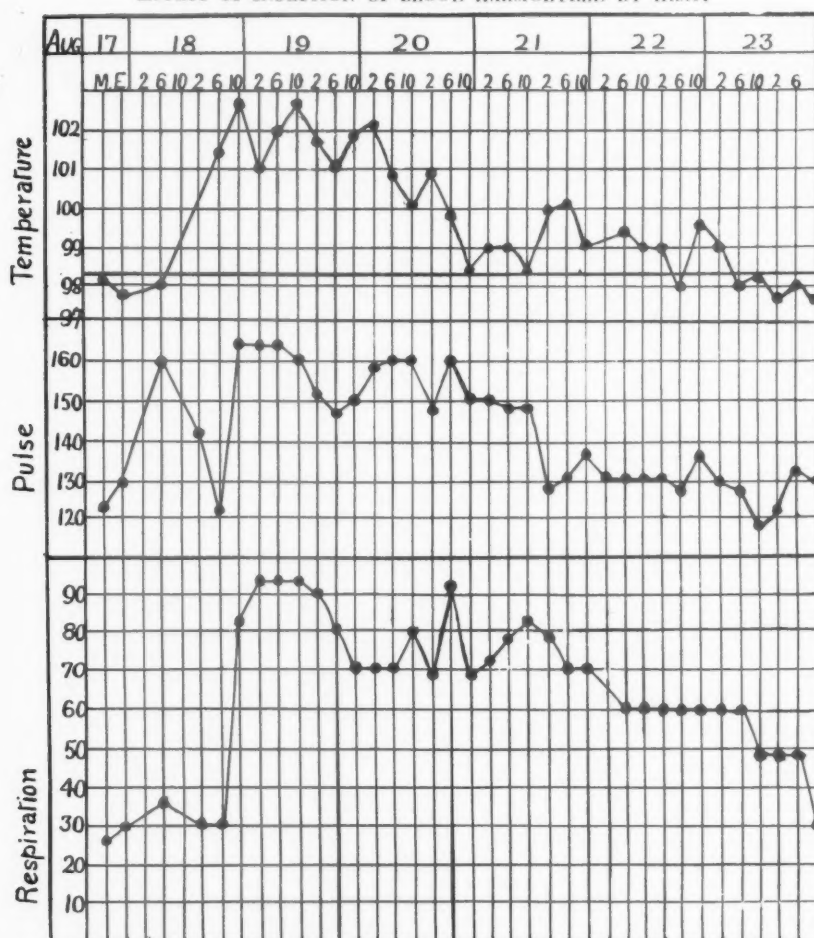
had formed at the site of each injection, there being no marked difference in the size of wheals. As a control similar tests were made on a patient suffering from Fröhlich's syndrome with identical results.

The effect of subcutaneous injection of heated blood.

Citrated blood, haemolyzed by heat, was injected in increasing doses into the subcutaneous tissues of a patient suffering from pink disease, and at the same time similar injections were given to a patient with mild nutritional anaemia as a control. The amounts injected were 2, 4, 10, and 12 c.c. at weekly intervals. The patient with nutritional anaemia showed no reaction. The patient with pink disease showed no reaction until the dose of 12 c.c. was reached. About eighteen hours later the pulse rate rose from 124 to 160 per minute. In a further twelve hours the temperature rose from the normal level to 103.8° F., and the respiration rate to over 90 per minute. There was collapse, sweating, and an aggravation of the swelling and pinkness of the hands and feet. No abnormal physical signs were detected in the lungs or elsewhere. This condition persisted for forty-eight hours, and terminated by lysis in a further four days, the patient eventually making a good recovery.

CHART II.

EFFECT OF INJECTION OF BLOOD HAEMOLYZED BY HEAT.



The reaction of this patient was so violent that it was decided not to make any confirmatory experiments. Her behaviour, however, taken in conjunction with the rise of mortality from roughly 20 per cent. in all previous cases to 60 per cent. in 1933, in which year the summer was abnormally hot, and with the death of a patient following accidental exposure to sunlight, suggested that heat was an important factor in causing the condition, and that cooling the patients would have a beneficial effect on the course of the malady.

Effects of cooling.

In 1934 twelve patients were admitted, and in all cases treatment was directed towards keeping the patients cool. The methods adopted to attain this end were:—

1. The patients were lightly clad, one garment only being worn. They were not covered by bedclothes.
2. Three times a day they were sponged with cold water.
3. An electric fan was placed in the room.
4. The patients, if they liked, were allowed frequently to immerse their hands in a bowl of cold water, as suggested by Rocaz³. The majority of them appreciated this greatly.

The results of this treatment were striking. The summer was if anything hotter than that of 1933, but of the twelve cases admitted only one died (8.3 per cent.). The fatal case was that of a patient who contracted an infective enteritis very soon after admission and died in five days. Another patient was apparently cured and discharged a fortnight after admission, in November. However, he relapsed in January, 1935, and was readmitted. His second attack was the worst example of pink disease ever seen by the author, the teeth falling out and gangrene occurring in both feet and the lower jaw. The patient eventually died in March. In view of the severity of the illness the resistance put up by this patient was remarkable. Table 1 shows the results of this method of treatment.

TABLE 1.

CASE	AGE IN MONTHS	DURATION OF ILLNESS BEFORE TREATMENT	RESULT	DURATION OF TREATMENT
A. M.	22	4 months	Cure	18 days
L. M.	9	1 month	Cure	5 weeks
T. G.	15	4 months	Cure	3 weeks
P. R.	9	2 months	Much improved	6 weeks
M. P.	8	1 month	Cure	3 weeks
B. L.	8	1 month	Cure	4 months*
P. P.	9	3 months	Cure	4 weeks
K. P.	7	1 month	Death from enteritis	5 days
J. M.	11	4 months	Cure	4 weeks
D. C.	7	1 month	Cure	4 weeks
M. M.	8	2 months	Cure	6 weeks
B. H.	12	1 month	Apparent cure	2 weeks†

* This was the patient in whom a relapse was apparently induced by the injection of heated blood. She was kept in hospital a long time to make sure that no further relapse occurred.

† This patient relapsed and died in March, 1935.

Discussion.

It is well known that physical agents such as heat and cold can act as toxic substances.

So long ago as 1916 Storm van Leeuwin and van der Made¹ showed that raising or lowering the temperature of a decerebrate cat above or below the optimum of 38° C. profoundly influenced the reflex excitability of the nerves. This was greatly diminished by only slightly raising the temperature, whereas considerable lowering was needed to produce any definite results. Similar results were obtained in the decerebrate frog.

Heymans² studied the effects of raising and lowering the temperature of the blood in the rabbit by interposing a U-tube which could be subjected to varying temperatures in a carotido-jugular anastomosis. By rapidly raising the temperature of the U-tube to 90° C. the rectal temperature of the animal rose to 39 to 39.8° C. By cooling the anastomosis the temperature fell, and could be again raised on further heating. After the third repetition the animal died in convulsions. But when cooling and heating of the blood was done gradually, rectal temperatures varying between 34 to 32 and 41 to 42° C. could be produced, and the animal invariably survived. If the rectal temperature was raised to 43° C., even if as long as three hours was taken to do it, death in convulsions was invariably produced; but if the rectal temperature did not exceed 42.2° C., and the anastomosis was subsequently cooled, the rabbit recovered. Cooling produced similar but much less marked results, mortal hypothermia being estimated at 18 to 20° C. Heymans considered that the toxic effects observed were due to the direct action of heat alone, and not to the destruction of the blood or to the formation of a chemical substance therein, for if the blood were heated to a temperature of 50° C. but cooled before its return to the body, no ill effects were observed. However, if the temperature of the blood were raised to 55 to 57° C., even though the rectal temperature only rose to 39.8° C., haemolysis occurred and the animal died with haematuria, haemoglobinuria, and parenchymatous nephritis. The heart and lungs were found to be able to stand their temperature being raised to 47° C. or more without apparent ill effect, so that it was assumed that the cause of death in hyperthermia was due to the effect of heat on the brain. Support for this hypothesis was forthcoming in an experiment in which the brain alone had its temperature increased (that of the trunk being only 35.2° C.), the animal dying in two minutes.

These experiments of Storm van Leeuwin and van der Made, and of Heymans demonstrate that heat even in small amounts acts as a toxic agent, and that the site of this action is in the nervous system. The hypothesis of the latter that it is due to heat alone and not to the formation of a noxious substance in the blood, cannot be accepted as proved, as possibly a thermolabile substance could be formed, which would cease to exist as such when the blood was returned to the body.

The toxic effects of heat, light, and other physical agents on man have been extensively studied by Dukes. Having first observed and reported a case of urticaria caused by light³, he collected a further series of cases of this affection which were apparently due to such causes as heat, light, cold, freezing, burns, mechanical irritation and physical and mental exertion⁷. Later, in an important paper⁸ he postulated a condition, akin to allergy, of heat-, effort-, and cold-sensitivity. He points out that heat may be regarded as a waste product, and that as an abnormal rise in the temperature in a given organ is damaging to its health and activity, so

an abnormal rise of the body temperature in general is damaging to the health and activity of the subject. Under normal conditions there is a remarkably efficient and complex mechanism which provides adequate cooling both of individual organs and of the whole body. Defective heat regulation may give rise to a variety of disorders affecting the body as a whole, or affecting the function of one of the internal organs, and finally may give rise to abnormal responses in one of the three important cooling surfaces—skin, nasal mucous membrane, and bronchial mucosa—and may cause serious pathological changes in these localities. Examples of general constitutional reactions are afforded by heat prostration and effort syndrome; of those referable to one of the cooling surfaces, thermic coryza, asthma (or more commonly a sense of oppression in the chest associated with cough, often complicated by a superimposed infection producing bronchitis), urticaria and eczema; of those referable to an internal organ, thermic headache or a gastric upset caused by a change of temperature or effort. The outstanding feature of all these disorders is that they can be brought about by heat, effort, or cold, as the case may be, and can be temporarily relieved by the reverse conditions.

Other skin affections observed by this author resulting from sensitivity to physical agents include erythema, itching, angioneurotic oedema, and, if the condition is chronic, desquamation. If to these manifestations be added nasal catarrh, depression, and prostration—all recorded symptoms of heat sensitivity—and the clinical picture so produced be transferred to the age of the first dentition, no one who has seen a typical case would hesitate to diagnose pink disease.

If it is assumed that pink disease is a manifestation of heat sensitivity, this would explain the seasonal incidence in this country. It would also explain the fall during midsummer and the rise at the beginning and end of the hot season, for according to Duke many heat sensitive subjects only react after previous exposure to cold. They become tolerant to heat during the summer, and lose their tolerance during the winter, so that the first warm days of spring produce a reaction. He further describes a type which reacts only after the first cold days of winter. These patients lose their tolerance to heat after a brief exposure to cold, and show symptoms during a subsequent warm spell.

Jeffreys and Ian Wood⁹ in a recent paper reject the theory that pink disease is an abnormal reaction to daylight because (i) they have found that patients who are nursed in the open air have a shorter illness than those who are nursed indoors; (ii) graded sun baths sufficient to produce tanning have been shown to be beneficial; and (iii) an analysis of 116 cases failed to show that the greatest number occurred at a time of year when the hours of sunshine were at a maximum. It should be noted that their objections are directed against the suggestion that light, not heat, is the responsible factor. If the disease is due to heat sensitivity it is easy to see why open air treatment is beneficial, while the benefit obtained by graded sun baths may well be due to a process of desensitization to heat; in fact it is directly comparable to the process of desensitization in ordinary chemical allergy, such as the injection of graded doses of pollen extract in hay fever. Lastly, the analysis

of the seasonal incidence of their cases shows a marked increase at the time when the days are beginning to lengthen after the winter, a fact which tends to support the hypothesis of heat sensitivity rather than to contradict it. Similarly Brown, Courtney, and MacLachlan¹⁰ found that no cases occurred in the summer or winter months, their seven cases being observed in April, May, June, and October. On the other hand, de Cosmi¹¹ found that the greatest incidence in eighty-nine cases was in the first six months of the year, sixty being recorded from January to May. The appearance of the affection during the cold weather may be due to the patients losing their heat tolerance during this time, and the onset may be determined by mistaken efforts to keep the child warm. Once even mild symptoms have developed the cold and clammy hands and feet and the perpetually running nose often cause the mothers to clothe the children warmly and to keep them in bed near a hot fire, which are disastrous measures for a heat-sensitive child. Possibly, too, some cases are due to the opposite condition of cold sensitivity, as is suggested by the following case (not included in this series):—

P. D., girl, aged nineteen months, was seen on December 17, 1935, for lack of vitality and weakness. She was the only child of healthy parents and had been fed on a 'humanized' dried milk, being apparently normal, for the first six months. At nine months she was given a mixed diet, although she never had gravy or meat, as her parents were vegetarians. She had, however, ample green vegetables, eggs, and milk. At six months, in December, she began to get weak and liable to attacks of depression. The hands and feet became red and swollen, and this was more obvious whenever the weather was cold. The hair began to fall out. The appetite remained good, there was no sweating, sleep was normal, and there was no nasal catarrh. The child picked up during the summer and had made good progress until the last few weeks, when there was a recrudescence of the swelling and redness of the hands and feet. The patient was seen on the first day of a period of cold weather, and the hands and feet were very red and swollen. The gait was rather unsteady and the child was fretful. Otherwise no abnormality was detected.

The above is admittedly a doubtful case, and the patient seemed convalescent. But it was difficult to diagnose any other condition than pink disease, and the dependence of the symptoms on a low temperature of the air was marked.

The nature of heat sensitivity in pink disease.

Although this investigation originated in observing the haemolytic effect of heat, it is obvious that in pink disease there is no haemolysis, as neither haemolytic jaundice, anaemia, or haemoglobinuria occurs, and in several cases a van den Bergh reaction was carried out with negative results. Moreover, the blood of patients with pink disease does not haemolyze at a lower temperature than normal blood. Morey and Michie¹² found that a patient suffering from a degree of heat sensitivity sufficient to cause urticaria, nausea, vomiting, palpitation, and fainting was much improved by injections

of histamine. Duke, however, found that sensitive patients react to heat applied to the forearm even when a tourniquet is applied to the upper arm, so that the production of a noxious chemical substance in the blood cannot be responsible. This is the same conclusion that Heymans came to as a result of his animal experiments. In pink disease there is apparently no marked skin sensitivity to heated blood, and although in the case reported in this paper a profound reaction followed the subcutaneous injection of heated blood, this was probably only a manifestation of hypersensitivity to serum injections in general, which according to Duke is characteristic of all heat-sensitive persons. It seems, therefore, most probable that all the tissues are sensitive to the direct action of heat, and that symptoms are more easily produced in the nervous system and in the cooling apparatus of the body than elsewhere.

The infective theory of pink disease.

The majority of observers consider pink disease to be due to infection by a specific micro-organism. The almost invariable association of the condition with catarrh of the respiratory tract, its appearance in this country only during the last fifteen years, its greater prevalence in some districts than others, and the liability to death from fulminating secondary respiratory infections are all suggestive of a specific infection. Nevertheless, many of these facts are explicable on other grounds. Cases may well have occurred previously and not have been diagnosed; the increase in incidence is synchronous with the increase in the popularity of sunbathing, and this appears to vary in different localities at different times, so that a condition of acquired heat sensitivity might assume the appearance of an epidemic. The liability to respiratory catarrh and to bronchopneumonia are just as likely to be allergic phenomena as manifestations of a primary infection.

On the other hand the following observations are highly suggestive that the condition is not due to infection:—

1. On the whole the illness is afebrile. The temperature tends to be unstable, with occasional rises above the normal line, but not to any degree. Any pronounced or prolonged pyrexia generally indicates the occurrence of a secondary infection.
2. The blood sedimentation rate was within normal limits in thirteen out of twenty-one cases. This fact almost precludes any active infection. It is suggested that an increased sedimentation rate points to a secondary infection.
3. Leucocytosis is not constant and the proportion of the polymorphs to mononuclear cells is not necessarily increased. The white cells per c.mm. were increased above the number of 12,000 in only sixteen of thirty-five patients.
4. No specific micro-organism has been isolated, and the bacteriological findings from the respiratory tract present no constant features.

Table 2 shows the white cell counts in thirty-four cases and the sedimentation rates in twenty-one.

TABLE 2.

CASE	PREVIOUS DURATION OF SYMPTOMS (MONTHS)	WHITE CELL COUNT PER C.MM.	POLYMORPHS. PER CENT.	BLOOD SEDI- MENTATION RATE
1	4	13,000	34	
2	5	16,000	64	16.25
3	1	7,187	21	
4	1	10,937	48	16.25
5	3	14,000	53	
6	2	18,437	64	11.25
7	1	15,000	80	
8	3	9,687	41	11.25
9	4	13,437	60	
10	1	10,396	36	3.75
11	1	23,437	68	4.9
12	2	9,060	44	16.25
13	2	8,442	49	13.0
14	2	28,124	49	21.5
15	2	16,250	65	
16	3	14,062	73	4.75
17	1	19,062	46	
18	1	9,375		5.25
19	3	17,187	64	
20	1	16,256	65	5.25
21	2	9,375	54	
22	2	5,937		2.8
23*	$\frac{1}{2}$	41,375	86	
24	2	5,077	68	
25	4	13,950	56	
26	1	13,437	38	
27	5	11,875	58	24.25
28	2	11,250	37	26.25
29	1			3.25
30	1	8,442	59	
31	3	8,442		10.0
32	4	7,500	69	2.75
33	2	7,500		3.25
34	2	10,937	50	3.0
35	1	11,260	27	1.0

* This patient was suffering from otitis media.

Thanks are due to colleagues in the pathological department, Dr. W. W. Mackarell and Dr. Mary Sharpe, for their help and advice, to Mr. C. J. Bond for his valuable assistance and advice in the experiments on haemolysis, and to successive house physicians who have so willingly carried out the routine work in connection with these cases.

Summary.

1. Pink disease occurs most frequently in the spring and late summer in this country.
2. One patient, previously reported, showed toxic symptoms on being placed in the sunlight, while another was accidentally exposed to sunlight through glass and died on the same day.
3. In the hot summer of 1933, six out of ten patients died, in spite of their being protected from the rays of the ultra-violet end of the spectrum.
4. In 1934, twelve patients were treated by cooling measures—hydrotherapy and light clothing. Only one case terminated fatally, death occurring from a ward infection five days after admission.
5. Blood in glass tubes exposed to sunlight was haemolyzed. This was proved to be due to heat rays. Blood haemolyzed by heat was shown to be highly toxic to a patient with pink disease when injected subcutaneously.
6. Adult patients with sensitivity to heat, effort, and cold show abnormal responses to these agents in the three important cooling surfaces of the body—skin, nasal and bronchial mucous membranes. All the symptoms described in adult physical allergy are present in pink disease.

Conclusions.

1. Sensitivity to physical agents, especially to heat, plays an important part in the production of the symptoms of pink disease.
2. Cooling the patients by light clothing, hydrotherapy, and keeping them out of direct sunlight greatly reduces the mortality and shortens the course of the disease.

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THE OXYDASE REACTION OF HUMAN MILK

BY

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Although it has been known for some time that ferments are present in milk, comparatively little attention has been devoted to the question. Not only the nature and source of these ferments but also their rôle in physiology is unknown, so that there is little wonder that their presence has not found any application in practice. Oxydase is a notable exception to this generalization. Since the publication of Raudnitz's work it has been known that this ferment is always present in colostrum. Since then much work has been done, especially by the French, on its presence in normal milk.

Of these latter workers Marfan is the chief, and he alone has made any attempt to use his findings for clinical guidance.

Marfan in his earliest researches was able to confirm Raudnitz's finding that oxydase was always present, and in considerable amount, in colostrum, and later he demonstrated that thereafter it gradually diminished in quantity, but that in at least 95 per cent. of examples it persisted to a certain small degree until the end of lactation, so long as the milk remained normal and the mother healthy. Marfan also showed that when the oxydase reaction in milk continues to be intense even for as short a period as eight days after parturition some suppurative process in the breast is most probably at work. This same author further found that an intense reaction might also occur when breast feeding is interrupted or when stagnation of milk is present. On the other hand, Marfan discovered that the ferment usually disappears from the milk when the secretion is very poor, or when lactation is at an end, and finally that the same may happen temporarily during menstruation.

Little more can be found in the literature. The present study was undertaken to supplement Marfan's findings.

Material studied

The milk of fifty women who were admitted with their babies to this Institution during the past year forms the basis of the present communication. The stage of lactation varied from the second week to the tenth month. Thirty-five of the cases were under observation for periods of at least two months, and in the remaining fifteen the period of observation was on the average two weeks.

Technique.—The test for oxydase was carried out in all the cases every third day, samples in the morning, at noon and in the evening always being examined. Three samples of milk were taken separately from each woman for each test; one before breast-feeding, one after breast-feeding and one

after the breast had finally been emptied by manual expression. Milk was obtained from both breasts so that the secretion from the two sides could be compared. All samples of the milk for examination were obtained by manual expression.

The test for oxydase was carried out immediately after the collection with 1 per cent. solution of guaiacol and hydrogen peroxide. The readings were made after the test tubes had been in the water bath at 50° C. for five minutes. The intensity of the reaction was recorded in the following manner: \pm incomplete, weak; + complete; ++ complete, moderate; +++ complete, intense; and ++++ complete, very intense reaction.

Results

As the basis for the interpretation of the results the first thirty-five cases in which the breast feeding remained uninterrupted during the whole period of observation have been taken. The results in the remaining fifteen cases, in so far as they were applicable, have been added to the general statistics.

TABLE.

SHOWING THE OXYDASE REACTION IN 35 NORMAL NURSING WOMEN CARRIED OUT SYNCHRONOUSLY IN MILK FROM RIGHT AND LEFT BREASTS DURING VARYING MONTHS OF LACTATION.

Case No.	MONTH OF LACTATION																		The daily average maximum quantity of milk (computed) c.c.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	
1	\pm	\pm	+	+															1170
2	\pm	\pm	+	+															900
3	\pm	\pm	+	+															1330
4	\pm	\pm	+	+															2000
5	\pm	\pm	+	+															1200
6	+	+	+	+															1400
7	\pm	\pm	\pm	\pm	+	+													300
8	\pm	\pm	+	+	+	+													800
9	+	+	+	+	+	+													1900
10	\pm	\pm	+	+	+++														1650
11	\pm	\pm	+	+	+++	+++	+++												1300
12	\pm	\pm	+	+	+	+	+	+++	+++										1400
13	\pm	\pm	+	+	+++	+++	+++	+++	+++										1450
14			\pm	+	+	+													700
15			+	+	+	+													950
16			+	+	+++	+++													1050
17			+	+	+++	+++													400
18			+	+	+++	+++	+++												600
19			+	+	+++	+++	+++												1600
20			+	+	+	+	+	+	+										2400
21			+	+	+++	+++	+++	+++	+++	+									1250
22			+	\pm	+++	\pm	+++	\pm	+++	\pm	+	\pm							1550
23			+	+	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++				1450
24					+++	+++	+	+	\pm	\pm									1500
25					+++	+++	+++	+++	+	+									2500
26					+++	+++	+++	+++	+++	+++	+++	+	+						700
27					+++	+	+++	+	+	+	+	+							1100
28					+++	+++	+++	+++	+++	+++	+++	+++	+++						2300
29					+	+	+++	+++	+++	+++	+	+	+						1000
30					+++	+++	+++	+++	+++	+++	+	+++	+	+++	+	+++			2450
31							+++	+++	+++	+++	+++	+	+						1450
32								+++	+++	\pm	\pm								1750
33									+++	+++	+	+							2900
34									+++	+	+++	+	+	+	+	\pm	\pm		1350
35									+++	+++	+++	+++	+	+	+	\pm	\pm		1800

R = right breast.

L = left breast.

In the first place it is seen from the table that oxydase was present in all the samples of milk tested. It may be mentioned in passing that out of 6,400 tests a positive reaction was obtained in all but five and in these latter other samples from the same mothers gave positive results.

It is also seen from the table that the oxydase reaction is, as a rule, equally intense in the milk from either side. The only exceptions are cases 14, 22, 27, 30, 32 and 34, but even in these cases the difference between the two sides is not great. It should be recorded that in case 22 an operation had been performed on the left breast during pregnancy. Although the secretion of milk was almost equal from both breasts after parturition, the oxydase reaction in the milk from the left breast remained less intense throughout the period of observation.

In order to ascertain whether there is any relationship between the quantity of milk secreted and the intensity of the reaction the total supply was measured and the daily average output determined. This latter figure is given in a separate column in the table and reveals that there is no constant relationship between these two factors. Hence the degree of the oxydase reaction cannot be taken as an index of efficiency in breast-feeding as some authors have asserted.

Perhaps the most striking feature in the table is the relationship between the intensity of the reaction and the period of lactation. In all cases the reaction became intense from the third month up till the six month of lactation, and thereafter gradually grew less intense.

Some authors have endeavoured to find out if there are other factors, outside the pathological conditions, which influence the intensity of the oxydase reaction. Marfan, for instance, maintains that the reaction is always most intense at the beginning of a breast feed. In forty-three per cent. of the present cases the reaction was most intense before suckling, in forty-seven per cent. after suckling and in ten per cent. the strength of the reaction was the same before and after suckling.

Milk is not constant in its composition. Indeed, variations in certain constituents occur from time to time during the day and in this respect the oxydase ferment is no exception. The cases which were under observation showed that sixty per cent. presented the most intense reaction in the evening, eleven per cent. in the morning and two per cent. at noon, whereas in twenty-seven per cent. the reaction remained constant in intensity throughout the day.

Marfan, as previously noted, maintains that interruption of breast-feeding leads to stagnation of milk in the breast and that in consequence there follows an increase in intensity of the oxydase reaction. The present cases, however, show that the normal nocturnal interval (eight hours) in breast-feeding is too short to produce any appreciable difference in this respect.

In addition to the above cases there has been an opportunity of studying the behaviour of the reaction during menstruation. At the beginning of the flow the reaction was very intense and then gradually became less so, but it never disappeared.

The test has also been carried out in five cases with mastitis. In all the reaction was similar to that obtained with colostrum and was particularly intense during the first forty-eight hours, afterwards becoming less marked. In one of these cases the number of leucocytes in the milk diminished in proportion to the diminution in the intensity of the reaction. In another example of mastitis, which was under observation, the reaction remained intense until the time of surgical intervention.

Finally, in seven cases of so-called genital crisis in the new-born, the test for oxydase was carried out in the liquid obtained from the breasts, and it was slightly positive in six and negative in one.

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EPITUBERCULOSIS

BY

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In 1921 Eliasberg and Neuland¹ suggested the new clinical conception termed epituberculosis. In young children with a positive tuberculin test extensive physical changes were found in the chest, consisting of an impaired percussion note with diminished or tubular breathing, mostly localized in the upper lobe, especially on the right side. Râles were only rarely heard. The general condition was comparatively good, the temperature was normal or slightly raised, the most striking feature being that in the majority of cases the physical signs, after remaining unchanged for some months, completely disappeared. This latter fact was not in accordance with the current opinion on the course and prognosis of extensive tuberculosis in young children. A progressive destructive process was expected. On account of this Eliasberg and Neuland concluded that the extensive physical changes appearing on the skiagram as a dense diffuse shadow were not due to specific tuberculous tissue changes. They suggested that these pathological alterations were a reaction in the adjacent lung tissue to toxins produced by a tuberculous focus. If the activity of the focus ceased these alterations might completely disappear. The infiltration should be put on the same level with the perifocal inflammation (Tendeloo) which may occur in the proximity of any inflammatory focus (e.g. the inflammatory swelling round a boil).

The clinical syndrome of epituberculosis soon found its way into the literature on tuberculosis in childhood. It served to give a better insight into the activity of the tuberculous process. This holds true especially since the conception of epituberculosis is used not only for the massive infiltration of a whole lobe but also for all kinds of diffuse shadows appearing suddenly in young children and disappearing again completely after a varying period. Epituberculosis as a clinical hypothesis is used to explain the existence of extensive tuberculous changes which cause no permanent damage in contrast with the hitherto-accepted bad prognosis of extensive tuberculosis in childhood.

The necessity of confirming this clinical hypothesis by morbid anatomical data has been urgently felt. It is obvious, however, that an occasion for post-mortem examination can seldom arise, as the most essential feature of these infiltrated areas is their complete restitution to normal. Publications on post-mortem findings are rare, none offering a convincing solution of the problem (Eliasberg and Neuland, Rubinstein², Grävinghoff³,

Harms and Klinckmann⁴, Pagel⁵). Many authors do not report on the anatomical structure, others mention serous, lymphocytic infiltration of the involved lung tissue.

In a child with a marked extensive tuberculous infiltration Spence⁶ punctured the lung in two different places twice in a month. The material obtained contained caseous tissue. Microscopically tubercle bacilli were found and on injection into a guinea-pig gave a positive result. Spence believes that the whole epituberculous infiltration consists of caseous tissue. Reichle⁷ assumes that epituberculosis is in many cases merely an extensive tuberculous pneumonia, differing from the ordinary type by undergoing complete reabsorption.

The rôle of atelectasis.

In the course of a study on the rôle of atelectasis in tuberculosis in childhood another explanation of the pathogenesis of the so-called epituberculous infiltrations seemed to suggest itself. In the author's opinion epituberculosis should be considered in many cases as atelectasis caused by occlusion of a main bronchus. In a former paper⁸ attention has been called to the occurrence of occlusion of a main bronchus during chronic lung disease in childhood. Especially in tuberculosis, which is characterized by swollen glands in the hilus, changing repeatedly in extent, occlusion of a bronchus may take place.

Atelectasis offers great difficulties in respect to its recognition by means of x-rays. Roentgenological evidence is clear in those forms of atelectasis in which a hitherto normal lung is suddenly occluded, for example, by the entrance of a foreign body. The air in the lung is quickly absorbed, so that a marked diminution of volume occurs (collapse of the lung). The diagnosis is more difficult if atelectasis takes place in the course of lung disease. In these cases the typical forms of collapse of part of the lung are not evident on the skiagram on account of the pre-existing shadows. Even so, if there is enough diminution of volume, it is possible to make a correct diagnosis, which may be confirmed by further skiagrams taken after reventilation has occurred. The diagnosis, however, is impossible if the occlusion takes place progressively. In these cases the lung gets filled with pathological material (drowned lung), so that atelectasis is not accompanied by diminution of volume of the lung. Moreover pleural adhesions may hamper the displacement of the mediastinum.

X-ray evidence.

It is not possible to give a description of all the x-ray evidence tending to confirm the hypothesis that epituberculosis should be considered in many cases as atelectatic in origin. It may be divided into the following five groups:—

(1) Skiagrams of epituberculosis showing the same picture as found in atelectasis. (2) Skiagrams showing a diffuse shadow in the lung field

together with displacement of the heart towards the involved side. (3) Series of skiagrams showing displacement of the heart occurring after increase of x-ray and physical findings. (4) Series of skiagrams showing decrease of physical and x-ray findings with simultaneous return of the displaced heart to its normal position. (5) Skiagrams of a case in which the shadow disappeared and returned again. At post-mortem examination the clinical diagnosis of atelectasis was confirmed.

Of each group a typical example will be given. The case mentioned in group 5 is more extensively reported as it seems to offer convincing proof for the thesis here put forward.

Case records.

Group 1. Patient A was aged one-and-a-half years at the time he was thought to be presenting a clear case of epituberculosis. The skiagram (fig. 1) showed a mottled shadow in the right hilus and



FIG. 1.—For full description of this and other illustrations see text.

the right middle field, with a homogeneous shadow of the right upper lobe. This shadow is clearly defined at the base by a line from the hilus laterally upward. This type of shadow is repeatedly observed if the bronchus of the right upper lobe is occluded by a foreign body (a similar case has been observed, in which the diagnosis was confirmed at autopsy). It may be surmised that in this very young child the tuberculous focus in the right middle field has caused a marked swelling of the glands in the hilum, which has brought about occlusion of the bronchus of the right upper lobe.

Group 2. Patient B, a boy aged two years, showed the clinical picture of epituberculosis of the right upper lobe. On x-ray examination (fig. 2) the heart was seen in the middle of the chest. The right border of the heart extended rather far to the right.



FIG. 2.

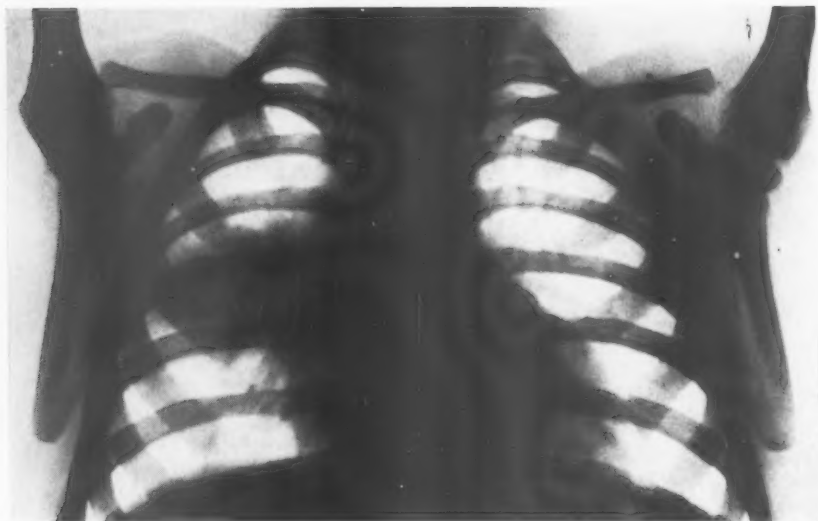


FIG. 3.

Caution is advisable in the interpretation of the position of the heart in young children as it is very variable. However under normal conditions the heart rarely extends so far to the right as in the case reported; in epituberculosis on the right side a similar displacement is repeatedly observed. Displacement of the mediastinum towards the involved side is generally either caused by collapse of the lung or by shrinking of the lung tissue.

As the latter condition is rare in the type of tuberculosis in which epituberculosis occurs, the conclusion seems justified that the x-ray evidence of displacement of the heart to the involved side must be accounted for by collapse of the lung. Increased translucency is shown at the base of the right lung as is often seen in the adjacent tissue in atelectasis.

Group 3. Patient C, a boy came to the hospital when two-and-a-half years of age. Physical examination revealed an area of slight dullness with diminished breath sounds between the scapula and the spine over the right lung. The first skiagram showed a homogeneous shadow on the right side with normal position of the heart (fig. 3). Some weeks later on physical examination displacement of the heart was found. The area of dullness had increased. The skiagram (fig. 4) confirmed the clinical diagnosis.

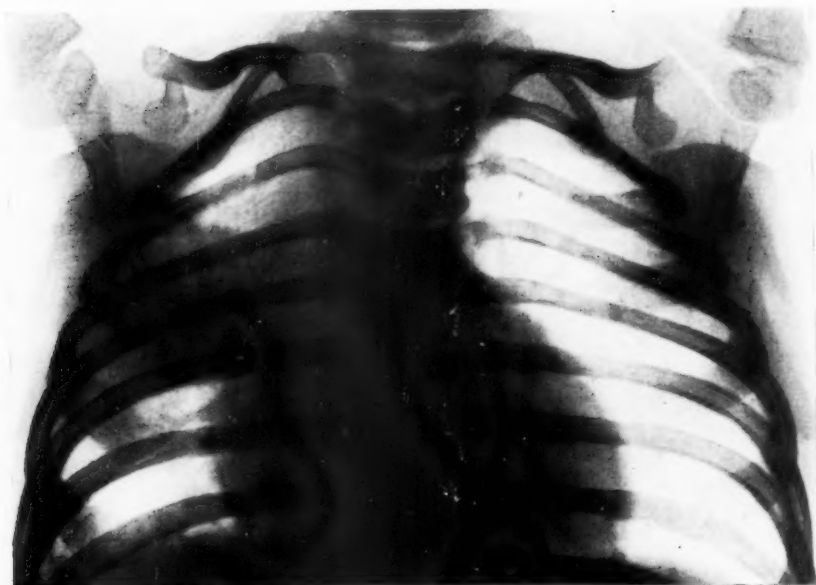


FIG. 4.

The trachea, which in the first skiagram was visible in the mid-line was now displaced to the right. The border of the heart extended further to the right. The size of the shadow had increased. The simultaneous incidence of increase of physical and x-ray findings in the lung with displacement of the heart makes it probable that this was a case of atelectasis with collapse.

Group 4. Patient D, an infant, was brought to the hospital when four months of age. The tuberculin test was positive. In the first skiagram taken on 26.iv.1934 (fig. 5) the left border of the heart was not visible and only a mottled density was seen. In the left upper lobe, close to the spine, a convex, dense diffuse shadow was seen. The right upper and middle field were entirely

opaque. This is one of the typical x-ray pictures of collapse of the right lung in which the heart is so much displaced to the right side that dextrocardia has developed. The next skiagram,

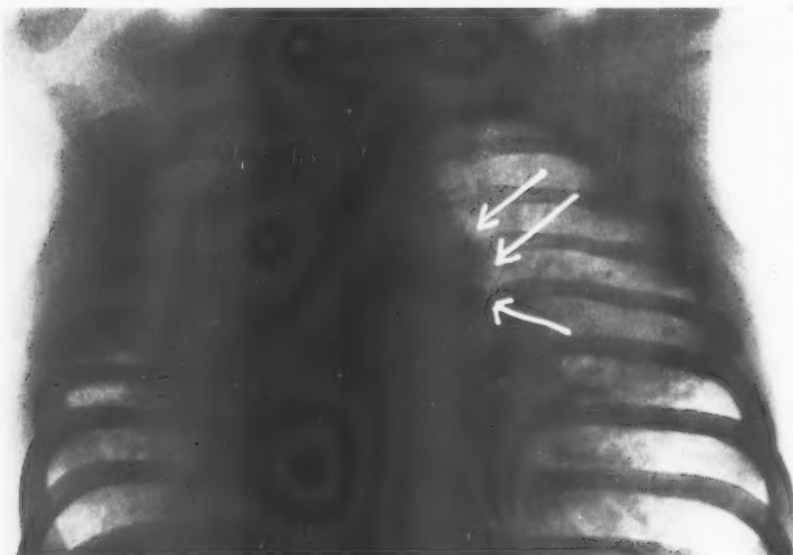


FIG. 5.



FIG. 6.

four weeks later (fig. 6), shows that the shadow on the right side had nearly disappeared. The remaining part of it was accounted for by an infiltration of the hilum accompanied by swollen glands. These pathological alterations had caused the collapse. The left border of the heart had returned to its normal position. The

convex defined shadow which was noticeable in the first skiagram was now overshadowed by the mediastinum. In this case the collapse made it possible to discern the shadow of a swollen gland, otherwise not visible on an antero-posterior skiagram. The child died (14.vi.1934) and at autopsy no remains of atelectasis were

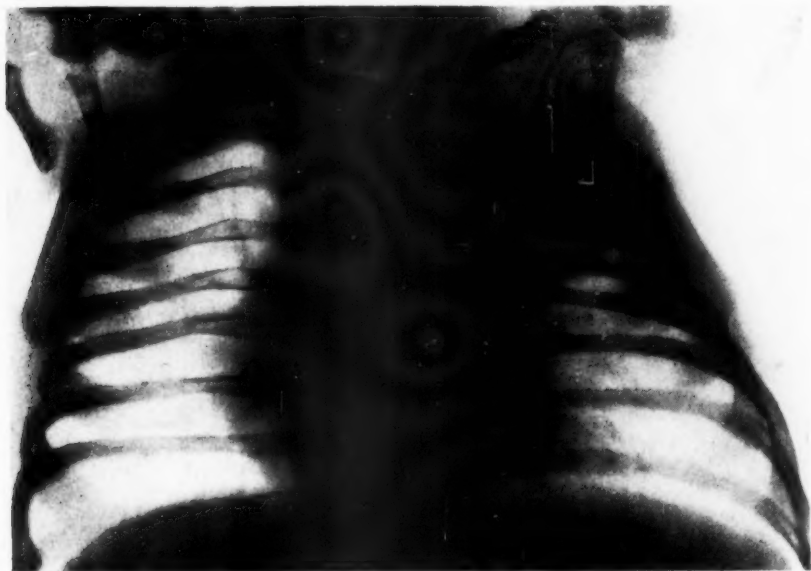


FIG. 7.

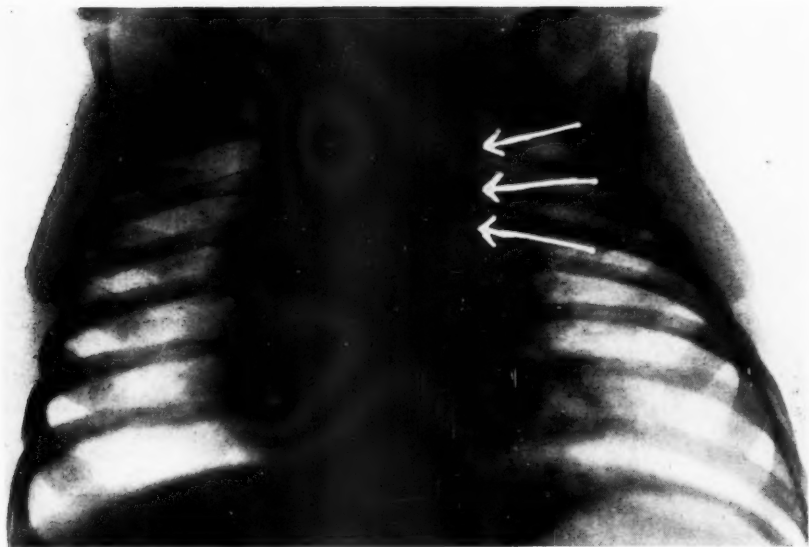


FIG. 8.

found. However this is no argument against the clinical diagnosis as the atelectasis had disappeared some time before death occurred.

Group 5. Patient E, a boy aged three months was admitted to the hospital on 20.ix.1934 suffering from tuberculosis. The first skiagram on 24.ix. (fig. 7) showed a homogeneous shadow in the

left upper lobe. This shadow gradually disappeared and a swollen paratracheal gland became visible on the left (fig. 8). The child contracted chickenpox, which activated the tuberculous process. The next skiagram (fig. 9) showed bilaterally swollen glands and again a homogeneous shadow in the left upper field. This shadow increased during the following days. The child became rapidly worse, clinical signs of tuberculous meningitis developed and death occurred on 9.iii.1935.

The x-ray findings in this case may be considered typical for epituberculosis. A homogeneous shadow in the upper lobe, disappeared and later reappeared when the tuberculous process was activated by a non-specific infectious disease.

From the findings at autopsy, kindly furnished by Dr. M. Straub, may be quoted the following essential facts:—

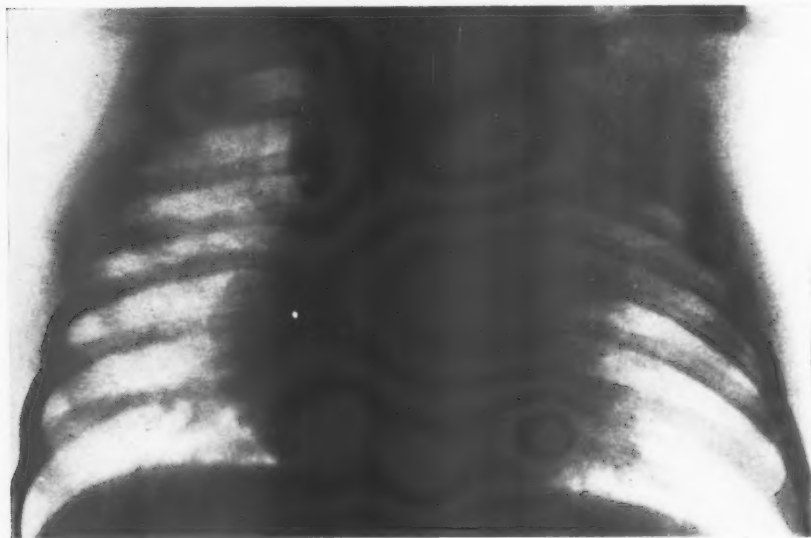


FIG. 9.

On section of the lower lobe of the left lung, below the centre of the posterior aspect of this lobe a subpleural yellow caseous focus was found, 1.5 cm. in diameter communicating freely with a bronchial branch and liquified in its centre (tuberculous primary focus). Round this focus the lung tissue showed a grey pattern of septa, and moreover a wedge-shaped portion was found here of a dark violet colour, extending up to 2 cm. from the pleural surface (atelectasis). The cranial third of the left upper lobe was relatively diminished in size, and on section showed a picture widely different from the adjacent lung tissue. It was of a greyish pink and showed a grey pattern of interlobular septa, which were widened. The lobules were small, and often showed a yellowish-brown, clover-leaf design, 1 to 2 mm. in diameter, and a minute grey reticular pattern. The bronchi in this portion was somewhat dilated. This abnormal lung portion was clearly demarcated from the normal tissue, the limit coinciding with a notch in the upper lobe surface (chronic atelectasis).

The broncho-pulmonary glands in the left hilum with the adjacent glands along the aortic arch and trachea were 0.75 to 1.5 cm. in diameter and completely caseous. A group of similar glands enclosed the bronchus that lead to the left upper lobe; one of these had perforated into the lumen of the bronchus, with an opening of 2 mm. (glandular component of tuberculous primary complex).

Of the microscopical picture the left upper lobe is of interest. Here the interlobular septa were found to be considerably widened by a loose connective tissue, with scanty cells. The lobules were small, as are the alveoli, the bronchi and bronchioles rather dilated and consequently salient in the picture. Round the bronchi and between the alveoli likewise an increase of connective tissue was found here and there. The alveoli contained numerous large vesicular cells, some of them with clear-cut vacuoles, some of the alveoli being crowded with them, locally mixed up with polymorphonuclear leucocytes. In some places the greatly narrowed alveoli had a lining of cubical epithelium. The bronchi and bronchioles were filled with a stringy mucus, containing shed epithelial cells and sometimes numerous polymorphonuclear leucocytes. The lining epithelial cells were normal in size and well preserved. Here and there some very small tubercles were found, composed of epitheloid and giant cells. The microscopical picture thus confirms the macroscopic aspect, namely, collapse of the lung tissue with indurative changes and indications of inveterate oedema. Acute pneumonic changes and tuberculous lesions remain in the background.

This autopsy record thus showed:—

1. The primary focus had grown into the bronchus, causing its obstruction and consequently atelectasis of the corresponding lung tissue. This proves that the clinical and x-ray changes which may be found round a primary focus, and often explained as a perifocal inflammation, must in some cases be ascribed to atelectasis.
2. The changes in the left upper lobe, which on valid considerations had been designed clinically as epituberculosis, proved to consist of atelectasis, caused by pressure of tuberculous glands on the bronchus.
3. The bronchi and bronchioles in the collapsed area were dilated. In anatomical sense bronchiectasis could be said to have already developed.

Discussion.

That the epituberculous infiltration is in some cases nothing else but atelectasis, is no new hypothesis. A search of the literature reveals many data pointing in this direction (Wallgren⁹, Kleinschmidt¹⁰, Engel and Segall, Beitzke, Duken). This applies equally to the massive extensive shadows, as to the small diffuse ones, which are at the present also considered to be indicative of epituberculosis. Some of these facts may be summarized here.

After the disappearance of the extensive epituberculous infiltration as a rule swollen glands remain in existence in the hilum on the involved side.

It is obvious that pressure of swollen glands on the main bronchus and lung tissue will occur in these cases. Wallgren states that in epituberculosis symptoms of stenosis of a bronchus are often present, the Jacobson phenomenon repeatedly being positive. On close examination of the skiagrams in some publications on epituberculosis (Langer, Kleinschmidt) a displacement of the mediastinum to the involved side is found. In the case described by Langer¹¹ the heart returned to its normal position after disappearance of the shadow. Cameron¹² reports that the shadow disappeared in a very short time. The same was observed in one of the patients under the author's care.

In a case of epituberculosis in an infant Fischl¹³ found atelectasis at autopsy. Further proof is offered by Morlock and Pinchin¹⁴. In their patient suffering from a typical form of epituberculosis of the right upper lobe, bronchoscopy was performed. In the right main bronchus, close to the bronchus of the upper lobe a tumour was protruding. By excision tuberculous glandular tissue was found. From the skiagram taken after bronchoscopy it appeared that the right upper field had become nearly clear. Only the lower branches of the bronchus of the upper lobe were still occluded. After two weeks the whole upper lobe was again opaque. After a week re-inflation had again taken place.

The question arises whether the clinical conception of epituberculosis can be dispensed with. Eliasberg and Neuland suggested it mainly because the good general condition and complete recovery were not in accordance with the prevailing opinion on the prognosis of tuberculosis in childhood. It has been repeatedly observed, that atelectasis complicating a chronic lung disease often does not affect the general condition in a marked degree. Moreover opinion on the prognosis of tuberculosis in childhood has much changed, especially in recent years. Complete recovery from extensive pathological alterations is no longer considered to be a great exception. On the other hand, a typical progressive destructive tuberculous process is sometimes seen developing in the same part of the lung as that in which formerly epituberculosis was diagnosed. In view of these facts there is less need for a specific explanation of cases like those described by Eliasberg and Neuland. Also from another point of view objections may be raised against the entity of epituberculosis. Post-mortem examination of children having died from extensive pulmonary tuberculosis never reveals a pronounced perifocal reaction, although in these cases large amounts of toxin are produced. Goldberg and Gasul¹⁵ have followed ten patients suffering from epituberculosis for more than two years. They leave the question open whether these pathological alterations should be considered as a perifocal reaction, or as caused by atelectasis or finally as not differing from other forms of tuberculosis.

It cannot be denied that the way in which the shadows in epituberculosis extend and disappear (for example, the phase of bipolarity) is not always identical with what has been observed in atelectasis. However, present knowledge of the clinical manifestations and x-ray findings in

atelectasis is limited. It has been obtained by studying cases of occlusion of a main bronchus, which is only a special form of this condition. Probably the clinical and x-ray findings will be different if a tuberculosis process is complicated by pressure of swollen glands on main and small bronchi and by direct pressure on lung-tissue.

Prozoroff¹⁶ has compared the shadows in epituberculosis with those in atelectasis in adults, suffering from tumours in the chest. He found a striking resemblance. Versé¹⁷ recently reported a case in which the shadows in the hilum, which were attributed to tuberculous foci proved at necropsy to be caused by atelectasis.

Occasional development of bronchiectasis in the atelectatic tissue is to be expected. Of this various cases are reported (Wallgren, Engel¹⁸, Rubinstein, case E in this paper). Children having recovered from epituberculosis should be followed during a long time as the clinical symptoms of bronchiectasis after atelectasis may reveal themselves sometimes after years (Anspach¹⁹).

Finally, it is possible that specific tuberculous tissue is present as well as atelectasis. A similar case was observed by Epstein²⁰. At the autopsy (performed by Ghon) the shadow proved to be caused by a primary focus with many tubercles in the proximity and atelectasis in the remaining part of the upper lobe.

Conclusions.

The clinical and x-ray findings in epituberculosis are often due to atelectasis. In other cases the infiltration consists of specific tuberculous tissue, resolving in course of time. A number of cases remain in which the pathological changes should be considered as a perifocal reaction around a tuberculous focus. Only clinical observation continued for a long time and post-mortem examination will reveal in what mutual relation these three conditions are occurring.

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ENCEPHALOGRAPHY IN THE INVESTIGATION OF CERTAIN CEREBRAL CONDITIONS IN CHILDHOOD:

PART I*

By Members of the Staff of the Royal Aberdeen Hospital for Sick Children.

This paper is a presentation and discussion of the information to be gained by studying the outline of the brain in a series of patients admitted to the Royal Aberdeen Hospital for Sick Children, in whom some cerebral defect was at least a possible diagnosis. The method chosen was encephalography, a procedure which aims at substituting air for the total volume of cerebrospinal fluid, and thereafter determining the distribution of the air, and of the cerebral tissues, by a study of skiagraphs. It was originally described by Dandy, and has proved to be of great value in the diagnosis of intracranial space-occupying lesions. Studies similar to the present investigation have been made by Crothers, Vogt and Eley¹ and by Guttman².

Technique of encephalography.

Preliminary examination of the patient.—It is essential that a careful preliminary physical and neurological examination be made of each patient. This must include an ophthalmoscopic examination, for one of the absolute contraindications to the use of the procedure is the presence of papilloedema. The presence of enlargement of the head is also an absolute contraindication, as pointing to an obstructive lesion in the posterior fossa of the skull. The examination also includes an assessment of any defect of intellect which may be present.

Anaesthesia.—Anaesthesia by a mixture of nitrous-oxide and oxygen with a trace of ether has been employed. It has been found entirely adequate, both for the surgical manipulations and for maintaining unconsciousness while the x-ray pictures are taken.

Technique.—The child is anaesthetized upon the x-ray couch. When anaesthesia is sufficiently deep, the patient is raised to the sitting position, and maintained in this by bending the body forward over a stool

* Part II will appear in the June issue. At the special request of the authors their names are not mentioned since the work was essentially that of a team.

(fig. 1). The head should be held forwards rather than backwards. The position has certain definite advantages: it permits the fullest possible



FIG. 1.—A child posed to show the position for encephalography.

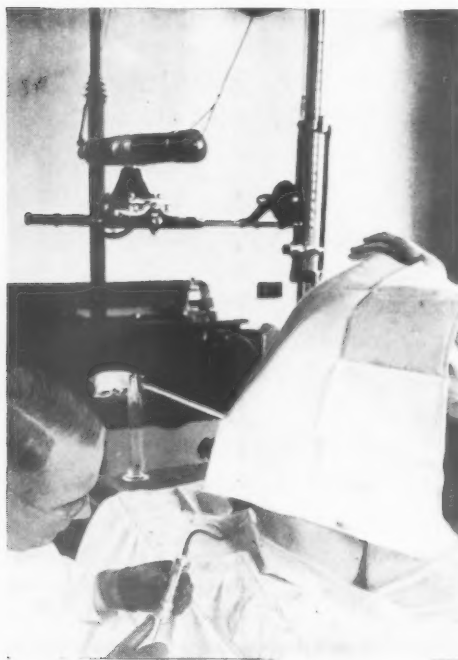


FIG. 2.—Technique of encephalography.

drainage of cerebrospinal fluid, it ensures that air shall rise to the depleted spaces, and it maintains an even distribution of the air over both halves of the brain. The air is introduced by lumbar puncture.* To the needle is

* For this, the shorter of the needles specially manufactured by Messrs. Weiss of Oxford Street, London, for injection of the branches of the fifth nerve, has been very satisfactory.

connected an adapter, and this leads to a 20 c.c. Record syringe through a length of four inches of thin, readily collapsible rubber tubing. The various fittings must be accurate so as to provide air-tight joints. The fluid usually flows freely; it is removed in amounts of about 10 c.c., and replaced by an equal quantity of air (fig. 2) drawn into the syringe through a filter of surgical gauze (fig. 3). For the average case, a sufficient allowance for the expansion of air at the temperature of the body is 2 c.c. for each 100 c.c. of fluid. This allowance is best made at the first substitution (i.e. 10 c.c. of fluid are withdrawn, only 8 c.c. of air injected). Forcible suction must not be used; it causes too rapid an upset in the balance of intracranial



FIG. 3.—Filtration of air before its injection.

pressures and, moreover, may drag a nerve root against the point of the needle, so that the flow stops. As a rule the weight of the plunger of a smoothly-acting syringe supplies all the suction that is necessary, and the merit of the thin rubber tubing in the connection lies in its collapse if the withdrawal of fluid tends to become hurried.

The attempt should be made to remove the fluid as completely as possible, and towards the end the child's head should be tilted backwards, to empty the dependent portions of the frontal horns of the ventricles. Finally, the plunger will move to and fro in the syringe, without exhausting any further fluid. In cases that have proved to be relatively normal radiographically, the average quantity withdrawn has varied from 50 c.c. to 80 c.c. A portion of the fluid is retained for chemical and cytological examination, the Wassermann test, and any further investigation considered to be desirable.

Radiographic technique.—Antero-posterior and lateral skiagraphs of the skull are taken previously. Encephalograms are taken with the patient supine, the desired position of the skull being maintained by a looped band passed round the head. This is kept taut by attaching to each end of the loop a sandbag weighing one pound. These are allowed to hang over the edges of the couch (fig. 4). Three views are necessary: an antero-posterior, taken with the head in maximum flexion, and right and left lateral views.

The technical details follow:—

TUBE: Victor X.P. 4.

DIAPHRAGM: Bucky, flat type.

FOCAL DISTANCE TO FILM: 30 inches.

EXPOSURE TIME: 1·5 seconds.

CURRENT: 30 m.a.



FIG. 4.—Method of maintaining position of head during exposure of film.

K.V.P. determined from table, after measurement of the antero-posterior and lateral diameters of the skull with the foot-measure used in shoe shops.

MEASUREMENT IN INCHES.						K.V.P.
4·4	50
4·7	52
5·0	54
5·4	57
5·5	59
5·7	61
5·8	63
6·1	70
6·4	72
6·7	75
6·9	77
7·4	77

After-treatment.--There is remarkably little reaction after the procedure. During the first one or two days, the temperature will be raised two or three degrees Fahrenheit, and some vomiting is usual. Headache is present for a similar period, but is easily controlled, especially if the child be not restless. It has been noted that the reaction to encephalography has been most marked in the cases in which gross cerebral defects were demonstrated in the skiagraphs. The foot of the bed is raised on blocks twelve inches high, a position which tends to free the medulla from the foramen magnum, and on the day after the procedure an enema of magnesium sulphate solution is given. By the fourth or fifth day all reaction seems to have disappeared. There has not been any mortality connected with the procedure and no undesirable after-effects have been observed. Indeed, as will be pointed out later in this communication, following encephalography the condition of the child is occasionally improved. If a space-occupying lesion is demonstrated, it will usually be best to proceed with craniotomy: for this reason the skiagraphs must be inspected before the child is returned to the ward.

The interpretation of encephalograms.

Although considerable experience is required in deciding whether a given encephalogram is abnormal, there are certain standards by which the normal is estimated, and it will be convenient to consider these at this point.

When the air reaches the cisterna magna, over the posterior surface of the medulla oblongata and vermis, it may be distributed in one or both of two ways:—

(1) It may enter the intra-cerebral ventricular system through the foramina of Majendie and of Luschka, and displace the fluid from the ventricles. In a majority of cases at least some air enters the ventricular system, but occasionally it fails to do so. It is important to understand that absence of ventricular shadows in the skiagraphs does not necessarily indicate the presence of a pathological condition, for it would appear that in most of such cases some minor anatomical peculiarity in the foramina leading from the fourth ventricle prevents the entrance of air, although it does not offer any obstacle to the normal circulation of cerebrospinal fluid. On the other hand, it happens occasionally that all the injected air enters the (usually dilated) ventricular system. This finding always indicates the presence of some intracranial pathological process, and it will be elaborated in a later section.

(2) The air may follow the extra-cerebral course of the cerebrospinal fluid, and pass in the median line by way of the cisterna pontis, cisterna interpeduncularis, and cisterna chiasmatis. From the last-named cistern five pathways debouch:—

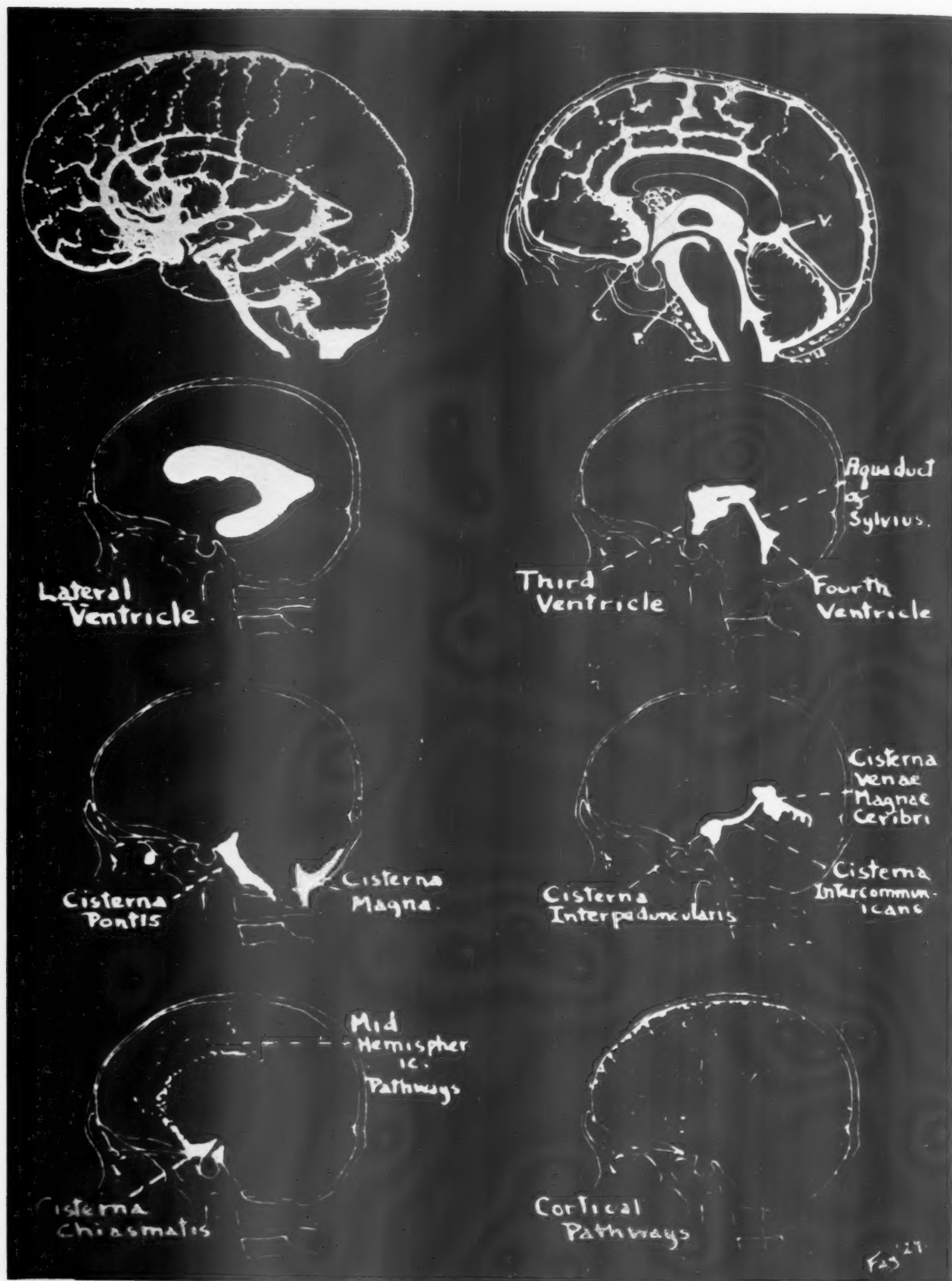


FIG. 5.—The distribution of air in the ventricular system and subarachnoid spaces, after Fay.

(a) Over the corpus callosum in the median line. (Unpaired.)

(b) Along the fissure of Sylvius and from thence over the Rolandic area and towards the vertex. From the Rolandic pathway there are



FIG. 6.—Normal encephalogram, antero-posterior view.
Compare fig. 5.

numerous offshoots; most of these pass over the frontal and parietal lobes and very few pass posteriorly over the occipital lobe. (Paired.)

(c) By way of the cisterna interpeduncularis and cisterna intercommunicans to the cisterna venae magnae cerebri. (Paired.)

The distribution of air in a perfect encephalogram is indicated in fig. 5 which has been constructed by Fay³; and the appearance of normal encephalograms is shown in fig. 6 (antero-posterior view) and fig. 7 (lateral view).

In the interpretation of an encephalogram, there should be examined in turn:—

(1) The size of the ventricles, whether increased on one or on both sides. Increase in size of the ventricles may be of an obstructive nature (fig. 8),

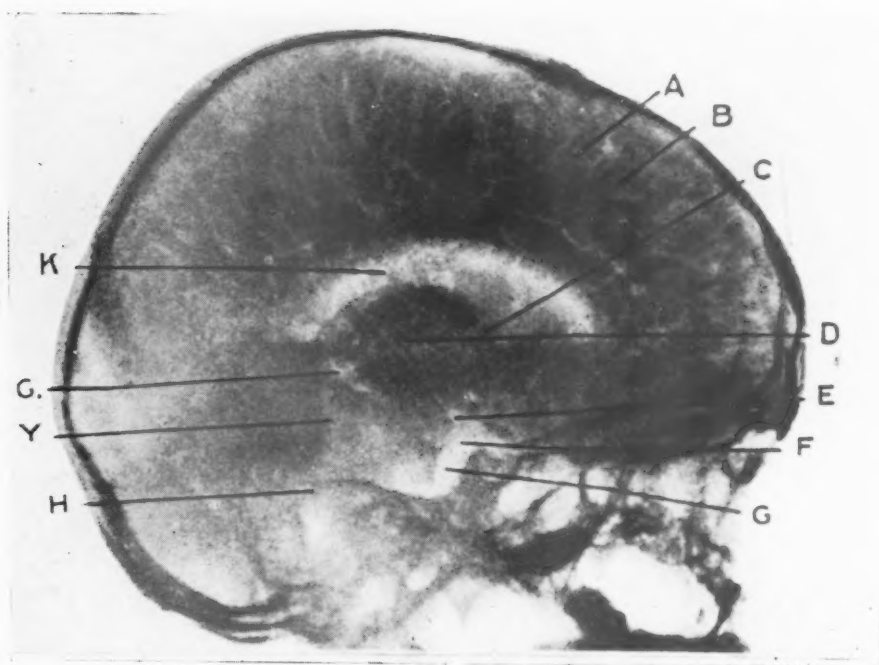


FIG. 7.—Normal encephalogram, lateral view (Pendergrass²).
Compare fig. 5.

due either to the presence of a lesion which prevents the free egress of cerebrospinal fluid, or to failure of the absorbing mechanism, so that the whole cerebrospinal circulation is stagnant. On the other hand, it may be of a compensatory type (fig. 9), and result from an attempt to take the place of an atrophic area of the ventricular wall. In the first type, the dilatation will obviously be bilateral and symmetrical; in the second, the dilatation is apt to produce a pouching of one ventricle, over an area

corresponding to the loss of cerebral substance, an appearance which has been termed 'wandering' ventricle. It is to be noted that space-occupying lesions in the hemispheres will produce lateral deviations of the ventricular system; but these are outside the scope of this paper.

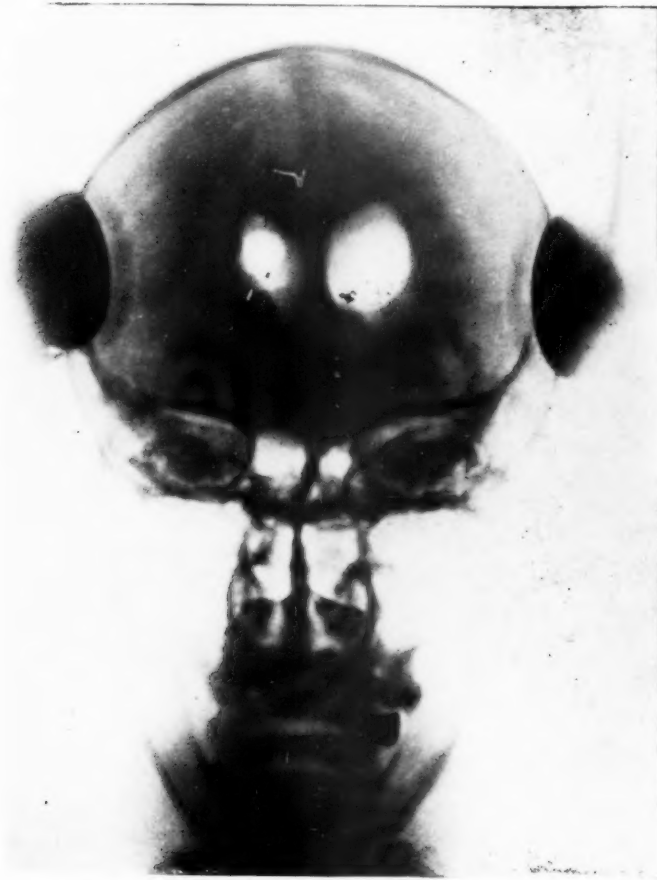


FIG. 8.—Bilateral symmetrical dilatation of lateral ventricles.

(2) The size of the basal cisterns, which is increased in cases of failure of absorption of the cerebrospinal fluid.

(3) The distribution of the pathways over the hemispheres; whether this is more extensive (for example, encroaching upon the occipital lobe), or partly absent, in areas of adhesive leptomeningitis.

(4) The width of the pathways over the hemispheres. Normally this is about 3 mm. When convolutional atrophy is present, it may be greatly increased.

Examples of these pathological appearances will be presented in the second part of this contribution.



FIG. 9.—'Wandering' ventricle on right.

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DIAGNOSIS OF PULMONARY MIDDLE LOBE DISEASE IN CHILDREN

BY

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In adults affections of the middle lobe of the lung although uncommon, are now well recognized. In children middle lobe disease is not only far more rarely seen but, owing to the fact that few or no clinical signs may be produced, diagnosis is rendered considerably more difficult. Indeed, as it is hoped to show in this communication, a correct diagnosis, and therefore efficient treatment, depends upon first, symptoms pointing to pulmonary disease and second, and as an immediate result of these, good x-ray pictures of the chest including lateral views. Particular stress must be placed on the latter and it must be emphasized that an ill child presents no insuperable difficulty, since both antero-posterior and lateral views, showing sufficient detail for an accurate diagnosis, can be obtained with a portable machine. Many of the skiagrams here published were taken in this way.

Radiological and applied anatomy.

The interpretation of x-rays taken to show the middle lobe, and particularly the interpretation of lateral views, depends upon an accurate knowledge of the radiological anatomy of that lobe and of the fissures which bound it. This perhaps can best be illustrated by means of diagrams and fig. 1 represents an antero-posterior view of the right lung with its fissures. Fig. 2 shows a strictly lateral view of the right lung and it is evident that in this view the middle lobe is approximately triangular in shape and that the base of the triangle rests upon both diaphragm and sternum. It will be shown that this relationship is unaltered when the middle lobe alone is affected by disease, so that diagnosis is possible merely from a consideration of the position of the base of the said triangle (see fig. 6 and 7). This is an important diagnostic point which does not seem to have been previously emphasized. In sharp contrast is the appearance seen in effusions occupying the interlobar fissures. Fig. 3 represents a lateral view of an effusion in the lower part of the large fissure. It will be seen that the base of the shadow rests entirely upon the diaphragm (see fig. 14). An effusion in the small fissure, however, produces a shadow with its base resting solely on the sternum. This appearance is represented in fig. 4 and a good example has been published by St. Engel and Schall¹. It must be realized that these figures are purely schematic since, as Sante² points out, the margins of an

interlobar effusion may be convex if the fluid is under sufficient tension to exert pressure upon the adjacent lung tissue. This, however, does not affect the importance of the position of the base of the shadow in the differential diagnosis between affections of the middle lobe and interlobar effusions.

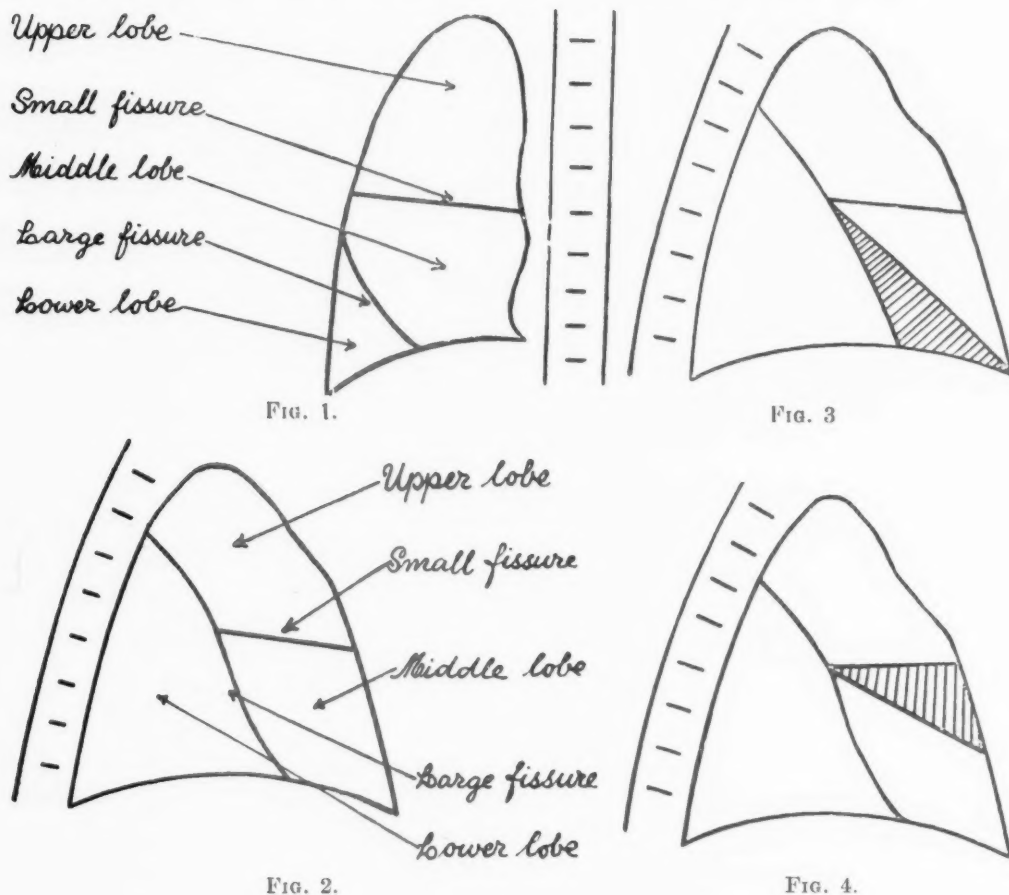


FIG. 1.

FIG. 3.

FIG. 2.

FIG. 4.

Diseases of the middle lobe.

The middle lobe of the lung is naturally subject to those diseases which affect the other lobes. These include, in children, pneumonia, collapse, bronchiectasis, epituberculosis and abscess. This communication is only concerned with those conditions affecting the middle lobe, which will produce a triangular shadow in the right mid-zone, and with their differential diagnosis. An abscess of the middle lobe does not produce a triangular shadow of this nature, and the authors have been unable to find any record of epituberculosis confined to the middle lobe or giving rise to this appearance. It is proposed to describe typical examples of the remaining three conditions.

Clinical records—(a) Middle lobe pneumonia.

Case 1. T. M., a boy aged five years, had previously suffered from measles, German measles and rickets. On the day of admission (26.12.35) his mother noticed that he was listless and feverish,

and he vomited once. His breathing became difficult and he complained of upper abdominal pain. On examination he was flushed: the respirations varied between 36 and 44 per minute and were grunting in character. The temperature was 103° F. and pulse rate 120. In the lower part of the axilla on the right

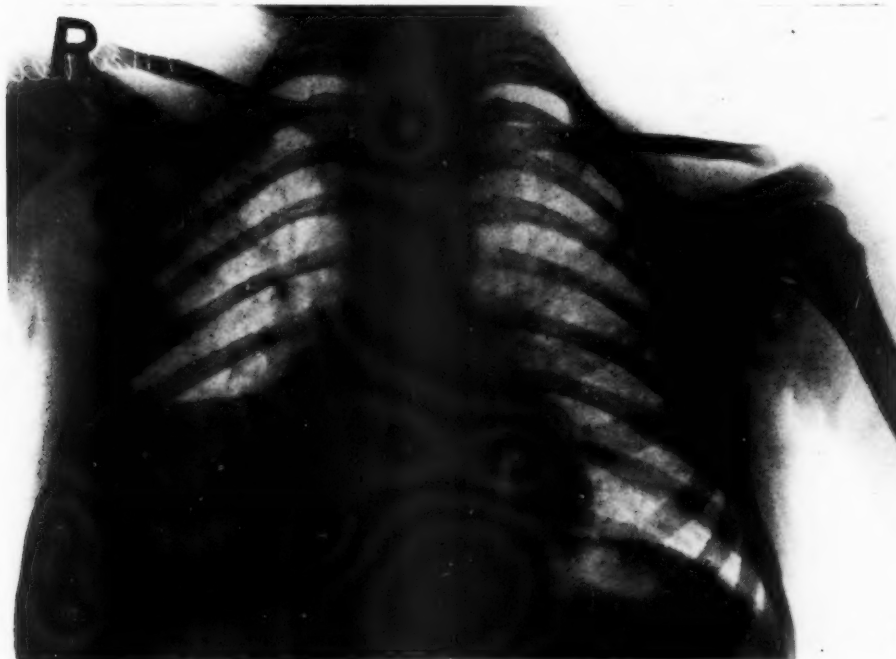


FIG. 5.



FIG. 6.

side there were fine râles and weak breath sounds and within forty-eight hours the classical signs of consolidation had developed. X-ray examination (30.12.35) shows in the antero-posterior view (fig. 5) a homogeneous opacity at the right base with a sharply defined upper margin, while the lower margin is less dense and is ill-defined. There is some enlargement of the hilar glands and slight displacement of the heart to the right. In the lateral view (fig. 6) there is a triangular opacity, with its apex directed towards the hilum, the base of the triangle being situated partly on the lower end of the sternum and partly on the diaphragm. The temperature remained sustained, the respiration rate varying between 40 and 64 per minute, until the fourth day, when a pseudo-crisis occurred. The true crisis was seen on the seventh day, following which the child made an uninterrupted recovery.



FIG. 7.

Further x-ray (7.1.36) showed that the opacity previously seen in the antero-posterior view had considerably cleared, no longer presenting sharp demarcation of its upper border and the heart has returned to its normal position. In the lateral view, however, (fig. 7) while the shadow is less dense, its borders are, if anything, more clearly defined and serve to demonstrate, in a beautiful manner, that the base of the triangle rests upon both sternum and diaphragm. The final x-rays taken on 13.1.36 showed complete resolution of the pneumonic consolidation with some residual interlobar pleural thickening.

Commentary.—Pfaundler and Schlossman³ state that in middle lobe pneumonia an antero-posterior view is sufficient for diagnosis, but St. Engel and Schall⁴ and Stoloff⁵ consider that lateral x-ray examination is essential

and with this the authors are in emphatic agreement. Reichle and York⁶ make a similar plea for the use of lateral views in the diagnosis of interlobar effusions.

(b) Middle lobe collapse.

Case 2. C. M., a boy aged eight years, whose previous history included measles and pneumonia at two, pertussis and bronchopneumonia at six and bronchopneumonia again at seven, had in March, 1934, at the age of seven, a further attack of pneumonia involving the right upper lobe. Following this he attended out-patients, but his cough persisted and led to an x-ray examination of his chest (7.5.34). This (fig. 8) shows in the antero-posterior view, a triangular opacity in the right mid-zone, with a sharply defined upper margin and an ill-defined lower one (c.f. fig. 5). Unfortunately, a strictly lateral x-ray picture was not obtained

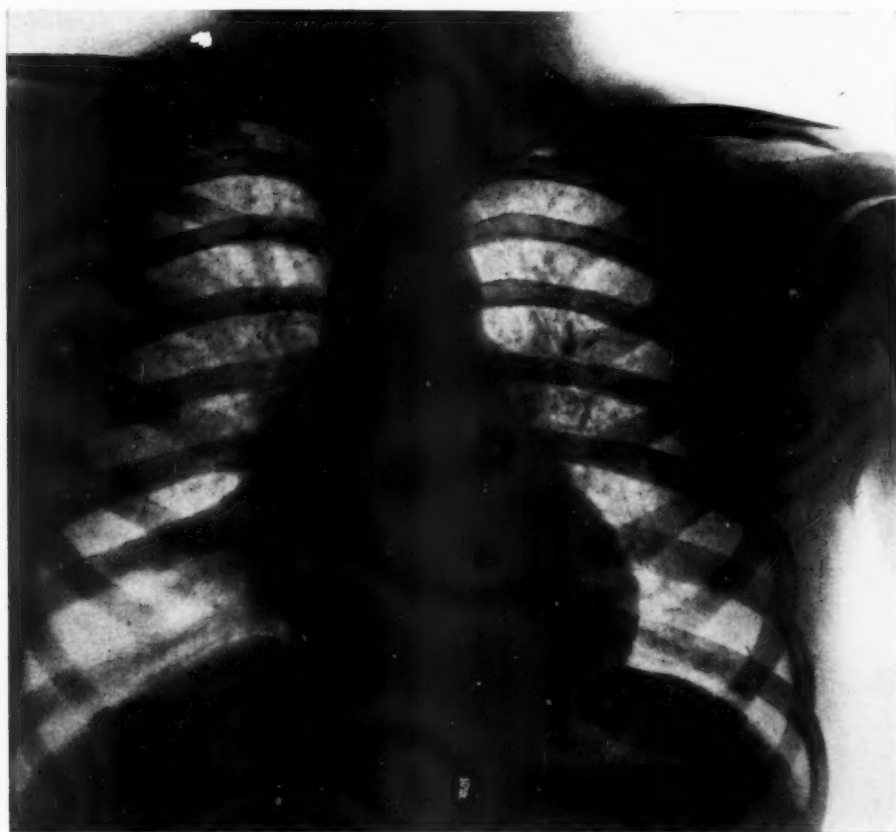


FIG. 8.

and the right anterior oblique view which was taken made it impossible to differentiate between middle lobe disease and an effusion in the small fissure. In actual fact, the latter was the radiological diagnosis made at that time, but a subsequent x-ray after lipiodol led to the suspicion of collapse of the middle lobe and bronchoscopy was therefore performed, when a plug of mucus was removed from the occluded bronchus. Ten days later a skiagram (fig. 9) shows complete re-expansion of the affected lobe.

(c) Middle lobe bronchiectasis.

As far as can be ascertained, bronchiectasis confined to the middle lobe has not been described in a child, although it might theoretically follow atelectasis due to obstruction of the bronchus. The following case is included, despite the fact that the bronchiectatic process is not limited to the middle lobe, because the antero-posterior x-ray (fig. 10) presented a triangular shadow in the right lung similar to that seen in the above two cases.

Case 3. A. S., a girl aged nine years, had pertussis at the age of five. This was followed by cough and sputum, the latter gradually increasing in quantity and at the present time amounting to 8 oz.

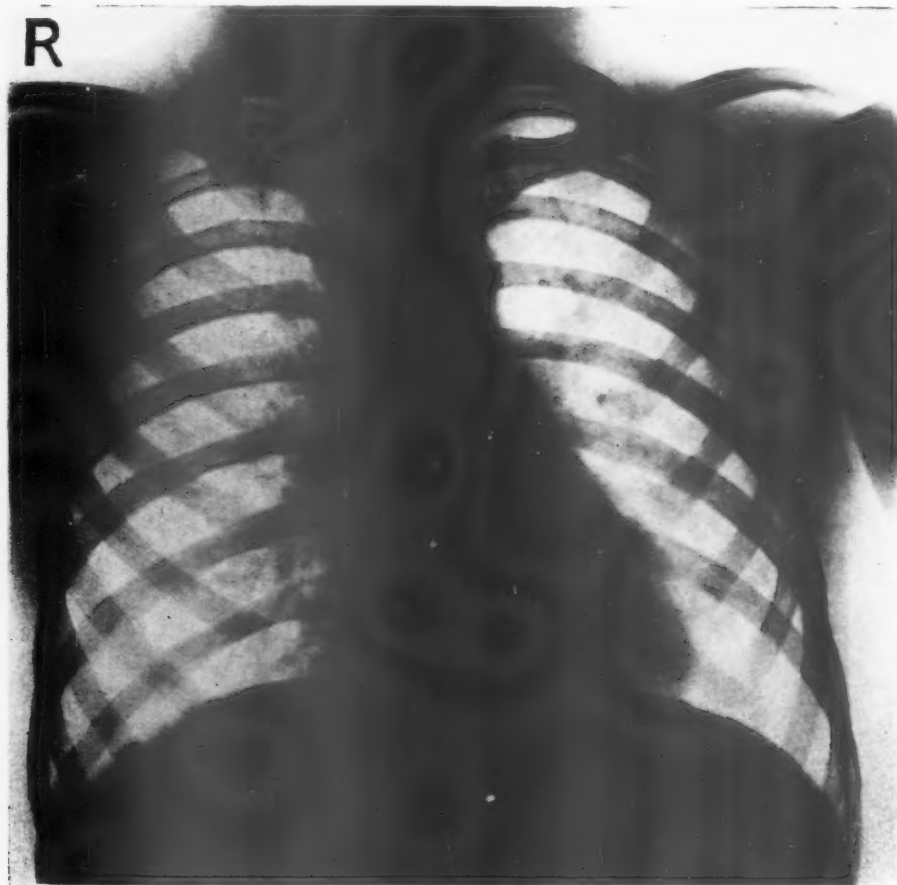


FIG. 9.

in twenty-four hours, purulent and of a foul odour. On examination there was clubbing of the fingers, at both bases the percussion note was impaired, the breath sounds were weak and accompanied by medium bubbling râles. X-ray examination (10.2.36) is pathognomonic of bilateral basal bronchial dilatation (fig. 10), but in addition, there is a triangular shadow on the right side, with a sharply-defined upper border, directed outwards from the hilum. The lower border is ill-defined (c.f. fig. 5 and 8). In the lateral view there is no sharp demarcation of this shadow. On 27.2.36 lipiodol was introduced in order to outline the right

bronchial tree. This confirms the presence of bronchiectasis (fig. 11), showing that both middle and lower lobes are diseased. The triangular shadow seen in fig. 10 is due to partial collapse of that part of the lower lobe supplied by the anterior branch of the lower lobe bronchus.

Differential diagnosis.

The conditions, other than those already described, which will produce a triangular shadow in the right mid-zone, include pneumonia affecting the lower part of the upper lobe or the upper part of the lower lobe and interlobar effusions, either in the large or in the small fissure. Pneumonia affecting part of a lobe, while it may produce, in the antero-posterior view, an appearance simulating middle-lobe disease, is at once differentiated by means of a strictly lateral examination, as will be realized from a



FIG. 10.

consideration of the radiological anatomy of the part. On the other hand, as a result of inaccurate radiological interpretation, interlobar effusions have often in the past been mistaken for middle lobe affections and vice-versa. It is suggested that such errors may be obviated if the radiological points emphasized in the earlier part of this paper are borne in mind. The following case illustrates some of the difficulties associated with a mediastino-interlobar effusion into the large fissure.

Case 4. B. M., a girl aged five, whose previous illnesses included measles and bronchopneumonia, was admitted in 1933, to hospital on account of loss of weight. X-ray examination showed enlarged mediastinal glands, and the Mantoux

tuberculin reaction (1:1,000) was strongly positive. On discharge she was sent to convalescent home and on her return attended the Middlesex Hospital Welfare Clinic. On 27.12.35, at the age of five, her mother said that the child was not eating, had a cough and complained of abdominal pain. It was found that she had lost over 2 lb. in weight since her last attendance three weeks previously. On examination she was pale and languid, but



FIG. 11.

presented no abnormal physical signs. The Mantoux test (1:1,000) was again strongly positive. X-ray examination of the chest (30.12.35) shows in the antero-posterior view (fig. 12) a triangular shadow, with a sharply-defined upper border and an ill-defined lower one (c.f. fig. 5, 8 and 10), the base being directed towards the heart. In addition, there is an inner triangular shadow lying against the mediastinum. This is bounded externally by a sharply defined margin, directed downwards and outwards. In a lateral view (not here reproduced) these two triangular shadows were continuous with each other, producing a quadrangle, the lower border of which rested solely upon the diaphragm. From what has been said previously, it will be evident that this appearance was not produced by an affection of the middle lobe, but was due to an effusion lying in the great fissure, part of the effusion being situated against the mediastinum. This condition may be described as a mediastino-interlobar effusion. That this interpretation is correct is proved by two

further series of x-rays. Those taken on 6.2.36 show, in the antero-posterior view (fig. 13), that the outer triangular opacity has now cleared, while, in the lateral view (fig. 14) the quadrangular shadow previously noted is very much smaller. In other words, the effusion in the large fissure has absorbed, but

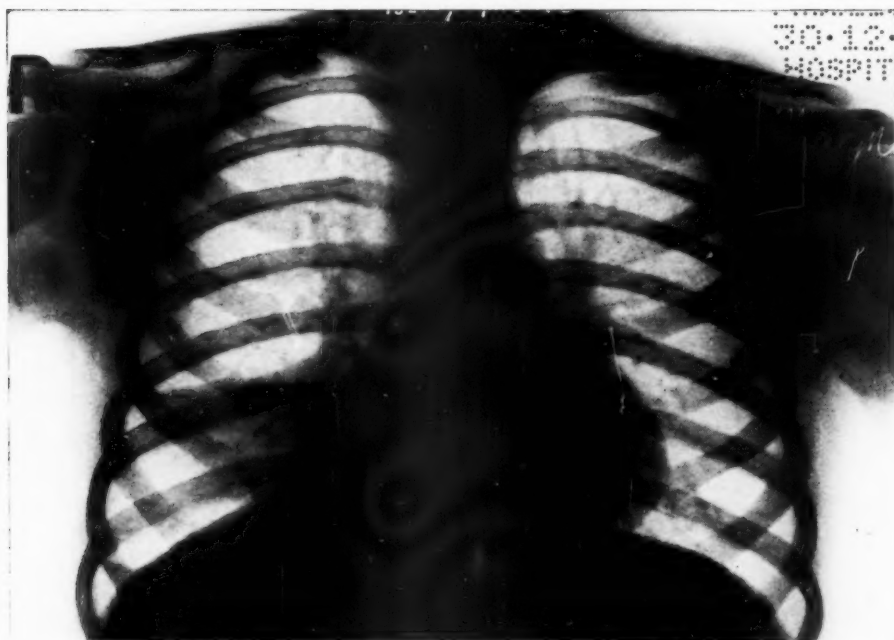


FIG. 12.

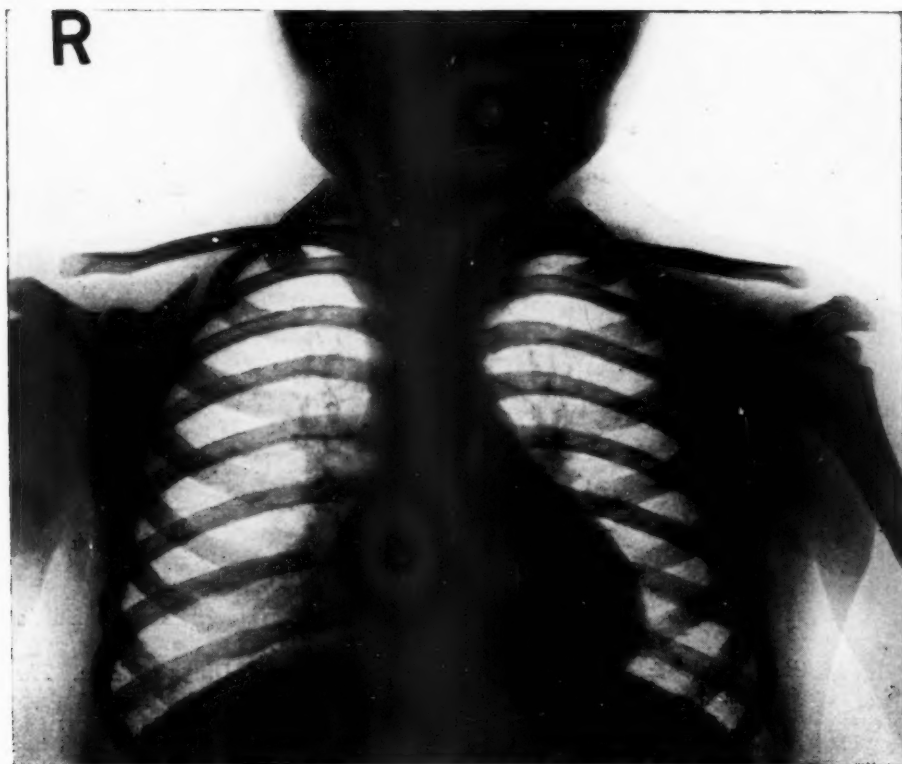


FIG. 13.

the mediastinal portion of the effusion remains. X-ray examination after lipiodol on 18.2.36 showed conclusively that there was no collapse of either the middle or lower lobes. The latter diagnosis might have been suggested by the shape of the inner triangular shadow in the antero-posterior views (fig. 12 and 13).

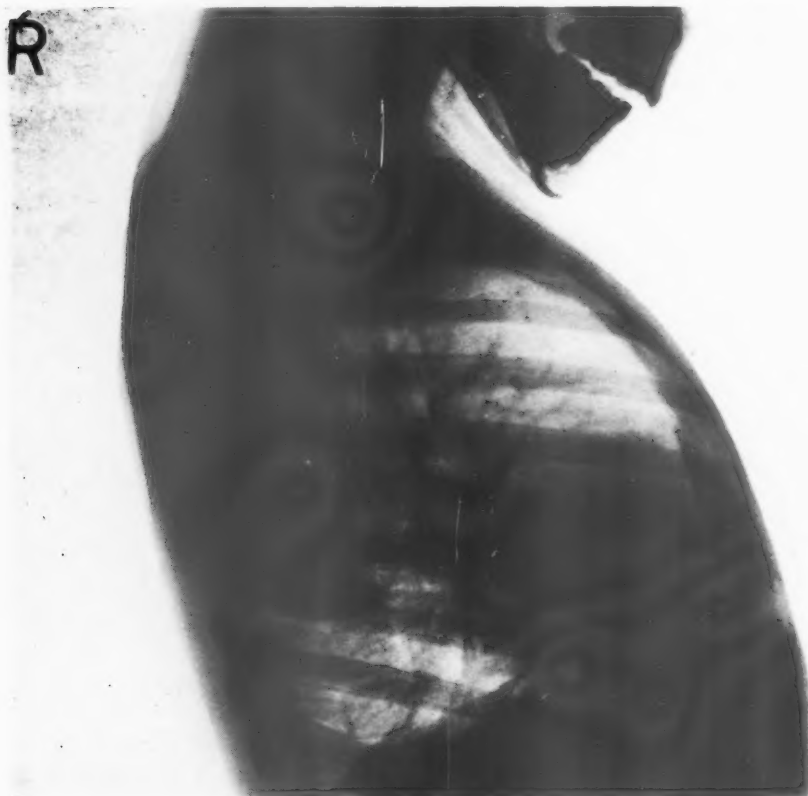


FIG. 14.

Summary.

1. The radiological and applied anatomy of the middle lobe and of the fissures which bound it is described.
2. The need for an accurate knowledge of this in relation to the differential diagnosis of middle lobe disease is emphasized.
3. Cases are described illustrating this and stressing the importance of good lateral x-ray pictures.

The authors' thanks are due to Dr. Graham Hodgson for his permission to reproduce the x-ray photographs in this article.

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ENCEPHALOGRAPHY IN THE INVESTIGATION OF CERTAIN CEREBRAL CONDITIONS IN CHILDHOOD :

PART II*

By Members of the Staff of the Royal Aberdeen Hospital for Sick Children.

The number of cases which have been investigated is forty-seven. In order to obtain more exact information it was necessary, in some cases, to repeat encephalography after a suitable interval, or (four cases) to supplement the information already obtained by ventriculography. In a second group of cases, encephalography was repeated as a therapeutic measure. Those cases involving multiple procedures will be referred to in the discussion. For convenience in analyzing the material, the cases have been arranged in four groups according to the 'reason for admission.' It is recognized that this grouping is arbitrary, and it will be noted that the diagnosis finally reached differed in a few cases from the tentative one. Nevertheless, the arrangement is convenient inasmuch as it reflects the problems that have confronted the general practitioners concerned. These four groups are as follows:—(1) Convulsions. (2) Epilepsy. (3) Mental defect. (4) Miscellaneous.

The protocols set out in sufficient detail the salient features of each case; positive information alone is included.

GROUP 1. CONVULSIONS.

Group 1 included eleven patients (see table 1), and in nine of these a lesion was demonstrated by encephalography; in six of the nine, the final diagnosis included mental deficiency. The lesions demonstrated in the group included:—

(a) **Atrophy of convolutions**, as a rule most marked in the frontomotor area. This varied in degree from a noticeable widening of the sulci as outlined by air, to gross loss of cortical substance.

An example of the former is seen in fig. 1 and 2 (H. D., 1935). The encephalograms demonstrate that the widening of the sulci is apparent not only over the site of normal fluid channels, but also over the parieto-occipital lobes. To compensate for the loss of substance a mild dilatation of the ventricular system has occurred. It is to be noted that the changes are general and strictly symmetrical; clinically the convulsions were generalized, and were invariably preceded by outbursts of temper. The radiological appearances are consistent with the presence of a defective absorbing mechanism for cerebrospinal fluid.

* Part I appeared in the April issue. At the special request of the authors their names are not mentioned since the work was essentially that of a team.

TAB

GROUP 1.

CASE	SEX	AGE	REASON FOR ADMISSION	NATAL HISTORY		BEGAN TO		AGE OF ONSET PRESENT STATE	PHYSICAL EXAM.	NEUROLOGICAL EXAM.
				NO. IN FAMILY AND PLACE	LABOUR	WALK	TALK			
D.L. 1933	M.	4 m.	Fits. ? Birth injury	5/5	Rapid	—	—	1 wk.	Head 14 in.	—
S.P. 1933	F.	5 yr.	Convulsions	3/2	—	1 yr.	1 yr.	3 yr.	—	Attacks of stupor
R.F. 1934	M.	1 yr. 10 m.	Fits. Loss of power left arm and leg	1/1	—	—	—	10 m.	Head 17 in. Rachitic	—
A.J. 1934	F.	3 m.	Fits ? Birth injury	1/1	Prolonged	—	—	5 days	Head 16½ in.	—
P.S. 1934	M.	5 yr.	Fits	10/8	—	14 m.	14 m.	6 wk. before adm.	—	—
W.W. 1935	M.	2 yr. 6 m.	Fits	8/6	—	1 yr.	2 yr.	1 yr.	—	Ataxic
W.R.F. 1935	M.	2 yr. 3 m.	Fits	1/1	—	—	2 yr.	1 m.	Deformity of both hands. Pes equino- varus	Very hypertonic weakness 6th nerve Lat. and rot. nystagmus
A.W. 1935	M.	3 yr. 6 m.	Fits. Unconscious	2/2	—	1 yr.	—	1 yr. 6 m.	—	Plantars extensor. All reflexes on rt. increased
H.D. 1935	M.	2 yr.	Fits	2/2	Rapid	1 yr. 4 m.	1 yr.	7 m.	Head 18¼ in.	Plantars extensor
E.M.P. 1935	F.	7½ m.	Fits	5/5	Very Rapid	—	—	4 m.	Head 16½ in.	Internal concomitant strabismus
W.T. 1935	M.	1 yr. 6 m.	Fits	4/3	Very Rapid	1 yr. 3 m.	1 yr. 3 m.	1 yr.	—	—

LE I.

CONVULSIONS.

OPHTHAL. EXAM.	MENTAL DEFECT	CONVULSIONS		C.S.F. REMOVED C.C.	FINAL DIAGNOSIS	ENCEPHALOGRAM AND REMARKS
		AGE AT ONSET	NATURE G = GENERAL L = LOCAL			
—	—	1 wk.	Right then G.	17	Chronic meningitis	Right—Marked cortical atrophy. Left—Adhesive arachnoiditis. Died 4 mths. later [P.M.]
—	Feeble- minded	3 yr.	G + cortical fits	49	Adhesive arachnoiditis	—
—	Yes	10 m.	L. (left) then G.	40	Amentia	Generalized arachnoiditis with secondary internal hydrocephalus.
—	Yes	5 days	G.	—	Birth injury	Atrophy of cerebrum, + in front. regions widening of subarachnoid pathways. Mild hydrocephalus. Block of absorp- tion. Died 6 mths. later [P.M.]
—	Noisy and destructive	5 yr.	G.	65	Congenital aneurism	All punctures gave blood followed by clear fluid.
—	—	1 yr.	G.	56	Idiopathic epilepsy	Non-expanding lesion in right fronto- parietal lobe. [P.M.]
—	Yes	1 m.	G.	85	Primary cerebral defect	Hydrocephalus 2/4, with wide sub- arachnoid markings. Suggests primary defect with microgyria.
Areas of choroido- retinitis L. fundus	Yes	1 yr. 6 m.	L. (Right)	58	Hemiplegia	Subarachnoid spaces prolonged over occipital lobes, excess of air on left. Some deviation of 'mid-line' to left. Fits began with pneumonia.
Discs rather pale	Yes	7 m.	G.	76	Amentia	Wide-spread cortical atrophy involving frontal and parietal regions with mild compensatory hydrocephalus.
—	—	4 m.	G.	62	? Amentia	Wide-spread convolutional atrophy in- volving frontal, parietal and occipital regions with hydrocephalus. Obvious marked cerebral defects.
—	—	1 yr.	G.	52	Recurring hypogly- caemia	Normal encephalogram. Fits due to recurring hypoglycaemia.

A more marked example of these generalized and symmetrical changes is seen in fig. 3 and 4 (W.R.F., 1935) in which the loss of substance is notable enough to suggest a primary cerebral defect of the nature of microgyria. In fig. 5 and 6 (D. L., 1933), an advanced degree of convolutional atrophy is strikingly apparent in the right side, the architectural arrangement having been reduced to four primitive convolutions of small size, the remainder of the cranial cavity on that side being occupied by air. This encephalogram also shows, on the left side, a complete absence of convolutional markings, to be attributed to an adhesive arachnoiditis over the left hemisphere. It is of considerable interest that the convulsions in this patient were right-sided, and that the gross reduction in the cerebral tissue of the right side had not given rise to any demonstrable paresis on the left. Some months later this child died of bronchopneumonia, and at autopsy the encephalographic findings were confirmed.

(b) **Arachnoiditis.** Fig. 7 (R. F., 1934) is an anteroposterior encephalogram, which shows complete absence of cortical markings over both hemispheres. In the opinion of the authors partial or complete absence of these markings is always a positive finding, indicating either obliteration of the subarachnoid pathways as a result of adhesion between the arachnoid and pia mater or the presence of a pathological barrier at the tentorium. In some of the cases an inflammatory etiology for this lesion has been forthcoming in a history of a previous attack of meningitis; in other cases, for example in the one here illustrated, the history has not given any clue to the cause or time of development of the lesion. The obliteration of the normal pathways in which cerebrospinal fluid ascends to the superior longitudinal sinus inevitably leads to serious interference with its absorption, and the resulting stasis of the fluid is reflected in the dilatation of the intracerebral ventricular system, as shown in the figure. Although the changes in this case appear to be symmetrical, the convulsions and weakness were most marked on the left side.

(c) **Hydrocephalus.** This appears in two forms. The dilatation of the ventricles may compensate for the loss of cortical tissue, when the process is a passive one; or it may result from obstruction to the normal circulation of cerebrospinal fluid, when the dilatation is an active one.

Fig. 8 (W. W., 1935) is an anteroposterior encephalogram which led one of the authors astray. The relevant clinical features in the case are available in the protocol. It will be noted that the upper part of the right lateral ventricle appears truncated as compared to the upper part of the left. This filling defect was noted, and was found to persist in a number of views. It was interpreted as evidence of a degenerative non-progressive lesion, possibly cystic, in the corresponding hemisphere. The area was

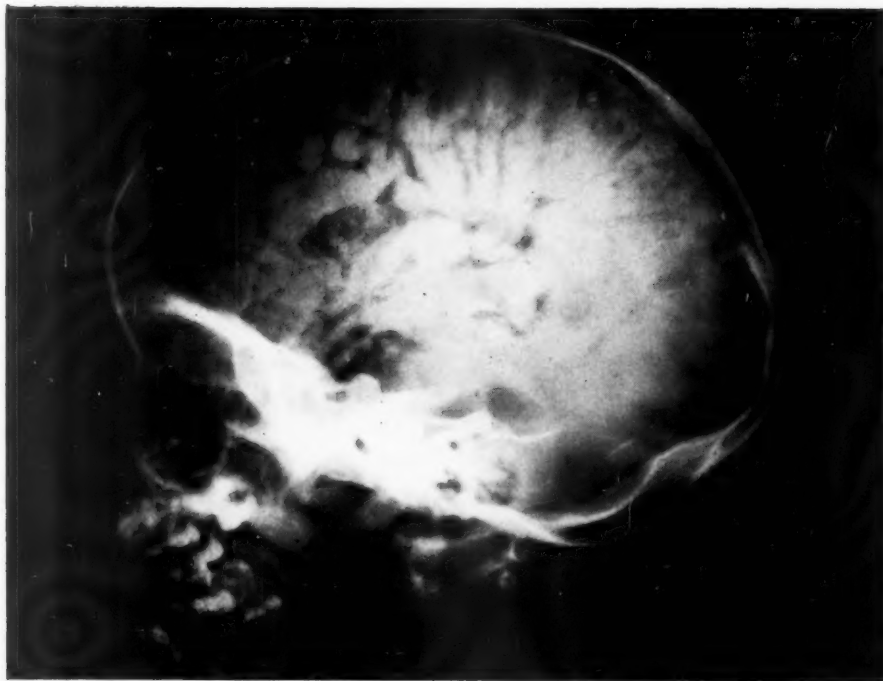


FIG. 1.—H. D., 1935.

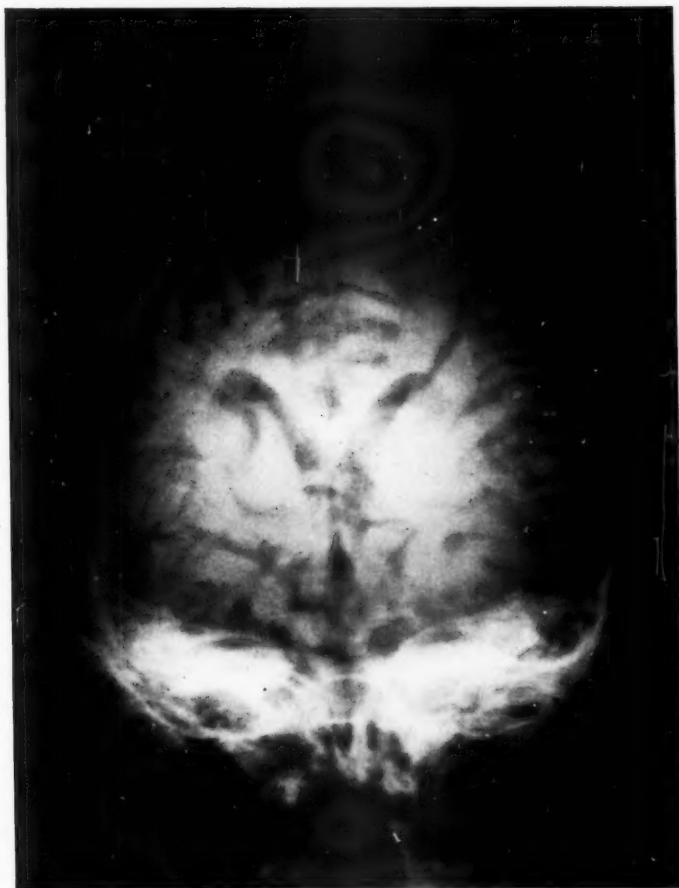


FIG. 2.—H. D., 1935.

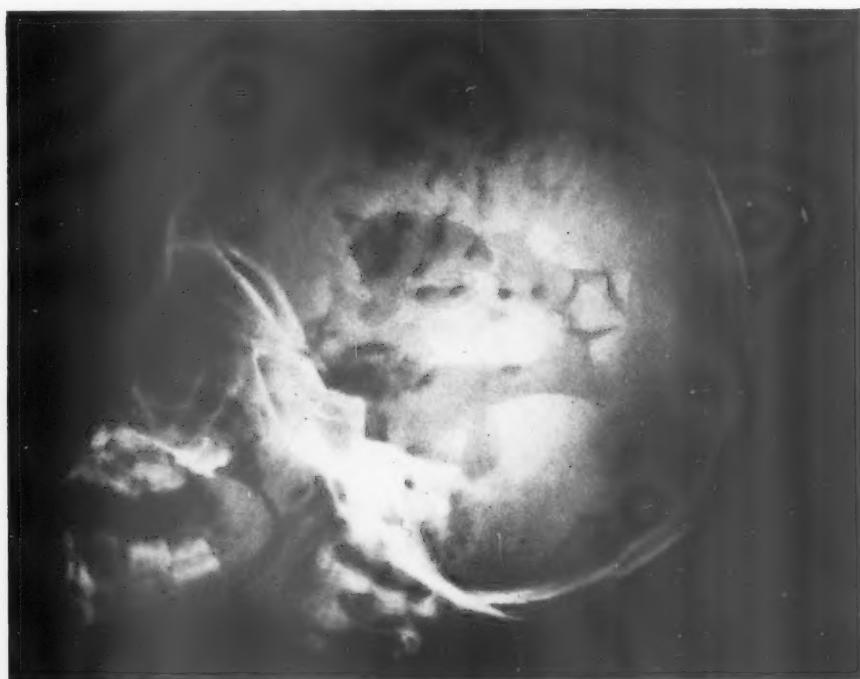


FIG. 3.—W. R. F., 1935.



FIG. 4.—W. R. F., 1935.



FIG. 5.—D. L., 1933.



FIG. 6.—D. L., 1933.



FIG. 7.—R. F., 1934.

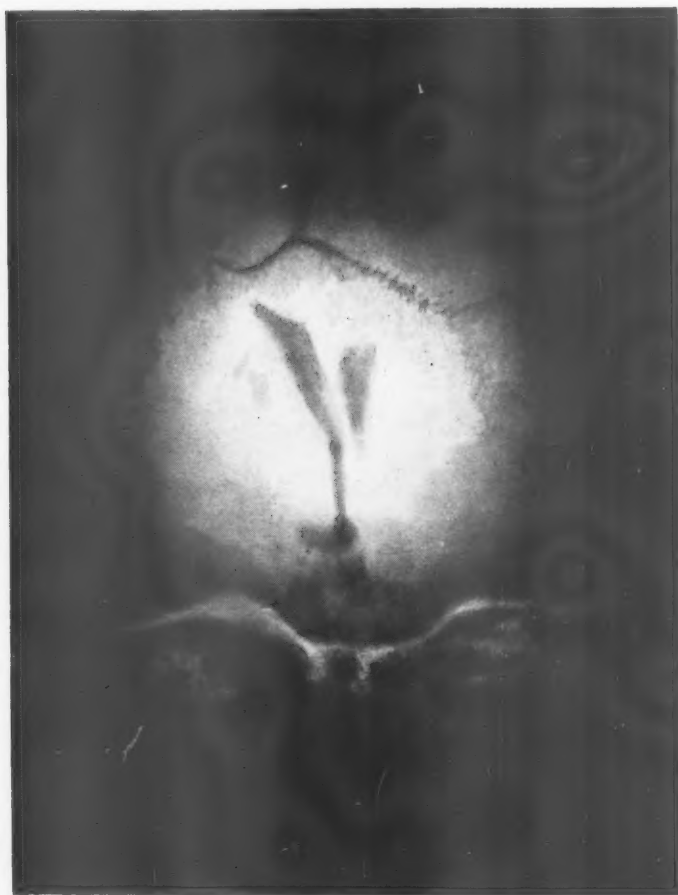


FIG. 8.—W. W., 1935.

explored by craniotomy, but no local lesion could be demonstrated. The child died, and the autopsy confirmed the absence of any lesion that might depress the ventricle.

The mistakes in this case were two in number: an error in the interpretation of the encephalogram, and an error of judgment in proceeding to craniotomy. The absence of lateral deviation of the entire ventricular system should have imposed caution in ascribing the clinical symptoms to a localized lesion.

In two cases in this group a lesion could not be demonstrated. In one (P.S., 1934) the recovery of blood-stained cerebrospinal fluid on repeated lumbar puncture led to the correct diagnosis of leaking congenital aneurysm; in the second case (W. T., 1935) the convulsions were ultimately found to be associated with recurring hypoglycaemia, and the encephalogram should have been unnecessary.

GROUP 2. EPILEPSY.

There were twelve cases in this group (see table 2). In five of these the encephalogram was abnormal. It has been found by Pendergrass (see ref. 3, part I) and others that in a certain number of 'epileptics' there is evidence of beginning of cortical atrophy, which is recognized by a widening of the sulci, especially in the frontal region. In other cases arachnoiditis is present, with consequent obliteration of the cortical pathways, and dilatation of the basal cisterns and ventricles. 'Epilepsy' is, however, merely a symptom, and encephalography must sometimes fail if it is employed to attempt to demonstrate a localized lesion. Moreover, the picture may be complicated by the appearance of intellectual degeneration which in at least a proportion of cases has a gross organic basis. Positive findings will therefore be of value both for diagnosis and for prognosis, whereas negative encephalograms do not materially assist in the elucidation of the individual problem; this is not an argument against the routine employment of encephalography, for each epileptic presents a problem to be studied in the greatest possible detail.

(a) **Cortical atrophy.** Fig. 9 and 10 (R. W., 1935) represent the accepted picture of so-called idiopathic epilepsy. The convulsions had been described as generalized but in hospital it was determined by close observation that the left side was first involved, though the convulsion became general almost immediately. The widening of the sulci is well seen, and the basal cisterns are proportionately enlarged; there is—as yet—little or no dilatation of the ventricular system.

(b) **Arachnoiditis.** In fig. 11 and 12 (J. C. McG., 1935) complete absence of cortical pathways is to be observed. The ventricles are well outlined and show the dilatation to be expected in the presence of stasis of

CASE	SEX	AGE	REASON FOR ADMISSION	NATAL HISTORY		BEGAN TO		AGE OF ONSET PRESENT STATE	PHYSICAL EXAM.	NEUROLOGICAL EXAM.
				No. IN FAMILY AND PLACE	LABOUR	WALK	TALK			
R.A.M. 1933	M.	9 yr. 9 m.	Epilepsy	2/2	Prolonged and asphyxia	1 yr.	2 yr.	4 m.	—	—
I.M. 1933	M.	6 yr. 10 m.	Epilepsy	1/1	—	1 yr.	1 yr.	1 yr. 3 m.	Small head	—
P.R. 1933	M.	10 yr. 6 m.	Epilepsy	4/1	Rapid	10 m.	1 yr. 6 m.	2 yr.	—	—
E.M. 1935	F.	5 yr.	Fits, in coma	2/1	—	9 m.	Late	—	—	—
R.W. 1935	M.	3 yr. 6 m.	Fits, epileptiform	1/1	Prolonged	—	2 yr.	1 wk.	26 lb.	L. side rather flaccid and sensation dim- inished. Congenital nystagmus
J. C. McG. 1935	M.	8 yr. 3 m.	Epilepsy	3/1	2½ mth. Premature (2¼ lb.)	1 yr. 3 m.	2 yr.	2 yr.	—	Plantars extensor. Reflexes diminished
A.C. 1935	M.	7 yr. 6 m.	Nocturnal fits	2/2	—	1 yr. 3 m.	3 yr.	—	—	—
M.S. 1935	F.	6 yr. 9 m.	Epileptiform fits	3/3	Prolonged shoulder presentn.	1 yr. 4 m.	1 yr. 6 m.	4 yr.	Anaemic	—
R.C. 1935	M.	8 yr. 6 m.	Nocturnal fits	2/1	—	11 m.	14 m.	7 yr. 6 m.	—	—
M.A.B. 1936	F.	3 yr. 6 m.	Nocturnal fits	6/3	Prolonged	1 yr. 6 m.	2 yr.	2 yr. 6 m.	Eczema	—
W.S. 1935	M.	10 yr.	Epilepsy	4/3	—	1 yr.	14 m.	1 yr.	—	—
I.F. 1935	M.	8 yr.	Epilepsy	1/1	—	11 m.	11 m.	2 yr.	—	—

LE 2.

EPILEPSY.

OPTHAL. EXAM.	MENTAL DEFECT	CONVULSIONS		C.S.F. REMOVED C.C.	FINAL DIAGNOSIS	ENCEPHALOGRAM AND REMARKS
		AGE AT ONSET	NATURE G—GENERAL L—LOCAL			
—	Degenerating	4 m.	G.	55	Epilepsy	Encephalogram negative. Ventriculogram negative
—	Now in Asylum	1 yr. 3 m.	L. often left sided	62	Amentia	Negative. Calcareous deposits in brain substance, right side
—	Degenerating	2 yr. Absent up to 6	G.	135	Epilepsy	General under-development of brain
Hyper- metropic (6)	—	—	L.	—	Epilepsy	Radiographic evidence of increased intra- cranial pressure
—	Yes	1 week	G.	118	Epilepsy	Widening of sulci. Basal cisterns pro- portionately enlarged
—	—	2 yr.	Both sides of face. Left limbs	70	Epilepsy	Complete absence of cortical pathways Ventricles well outlined Hydrocephalus 2/4
—	—	—	—	74	Epilepsy (Diencephalic)	Possibly slight dilatation of ventricular system, otherwise normal. Blood sugar .067 per cent.
—	—	4 yr.	G.	58	Epilepsy	Normal. Blood sugar .069 per cent.
—	—	7 yr. 6 m.	G.	80	Epilepsy	Normal
—	—	2 yr. 6 m.	G. infrequent	75	Epilepsy	Normal. Blood sugar .062 per cent.
—	—	2 yr.	G.	—	Epilepsy	Absence of subarachnoid markings. Hydrocephalus
—	—	2 yr.	G.	64	Epilepsy	Normal

the cerebrospinal fluid, the dilatation including the third ventricle. This patient provided an illustration of the occasional benefit that follows encephalography. It is thought that the introduction of air may lead to the sundering of meningeal adhesions, with consequent improvement in the circulation and absorption of cerebrospinal fluid. It must be pointed out, however, that the absence of cortical air markings need not necessarily be interpreted as obliteration of cortical pathways, for adhesions about the tentorial notch, a well-recognized pathological lesion, may arrest the progress of the air towards the hemispheres. Any beneficial effect from encephalography might be due either to the rupture of a localized barrier at the tentorium, or to the re-establishment of the lumen in cortical pathways, or to both these factors. In the case illustrated above, although the treatment remained the same before and after encephalography, the number of convulsions was strikingly diminished after the procedure. This is by no means a solitary example. It is quite impossible to predict which patients will benefit, although after the plates have disclosed a barrier in the cerebrospinal fluid channels the propriety of a second air-replacement procedure may well be considered. Indeed, parents have requested that this procedure be done; and it is significant that in one patient the request was instigated by the patient's teacher, who had observed marked improvement after the first encephalography. When a second encephalogram has been decided upon as a therapeutic measure cautious 'over-inflation' of the subarachnoid space by as much as 20 c.c. of air has been attempted in several cases. This was retained for about one minute and then scrupulously removed.

Fig. 13 (R. C., 1935) is an anteroposterior encephalogram which raises an interesting point in diagnosis. It will be observed that only one lateral ventricle has been occupied by air. However, in the absence of any lateral deviation of the ventricular system, this picture has been regarded as normal, and the appearance has been ascribed to some anatomical peculiarity of the corresponding foramen of Monro. The peculiarity has been encountered twice in the present series, and the normality of the ventricles in these cases has been demonstrated by a subsequent ventriculogram.

GROUP 3. MENTAL DEFECT.

In the group of mental defectives there were seventeen patients (see table 3). No attempt has been made to assess the degree of deficiency present in each case, and indeed in the case of infants no such attempt is possible. Broadly speaking, however, it may be stated that in this group are included those patients who could never be expected to be useful in a community. In only one case were the encephalograms normal; in the remaining sixteen the lesions demonstrated were often gross in nature, sometimes to a degree that could reasonably be described as astonishing. As a rule some

(continued on page 113)

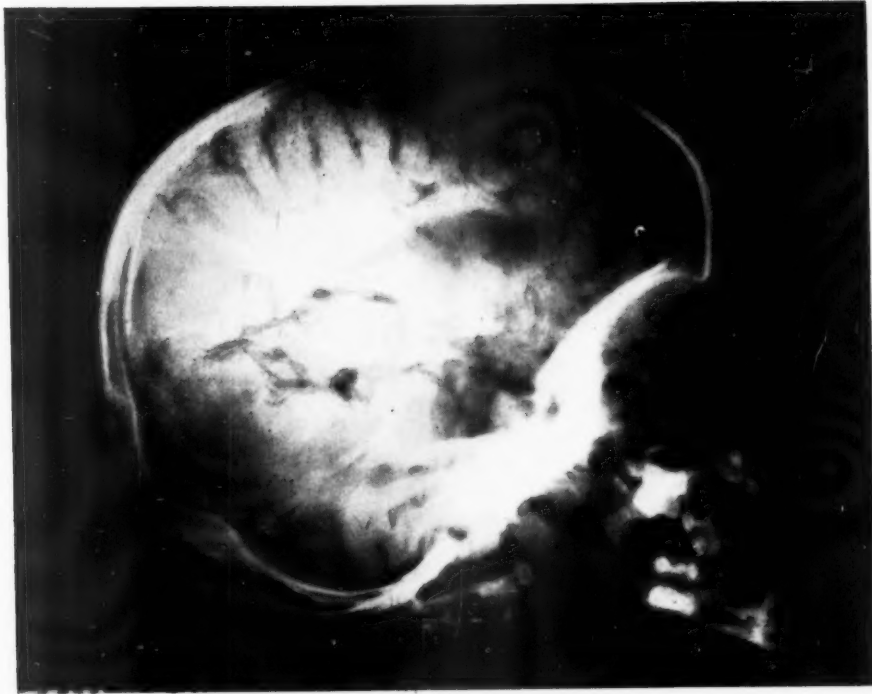


FIG. 9.—R. W., 1935.



FIG. 10.—R. W., 1935.

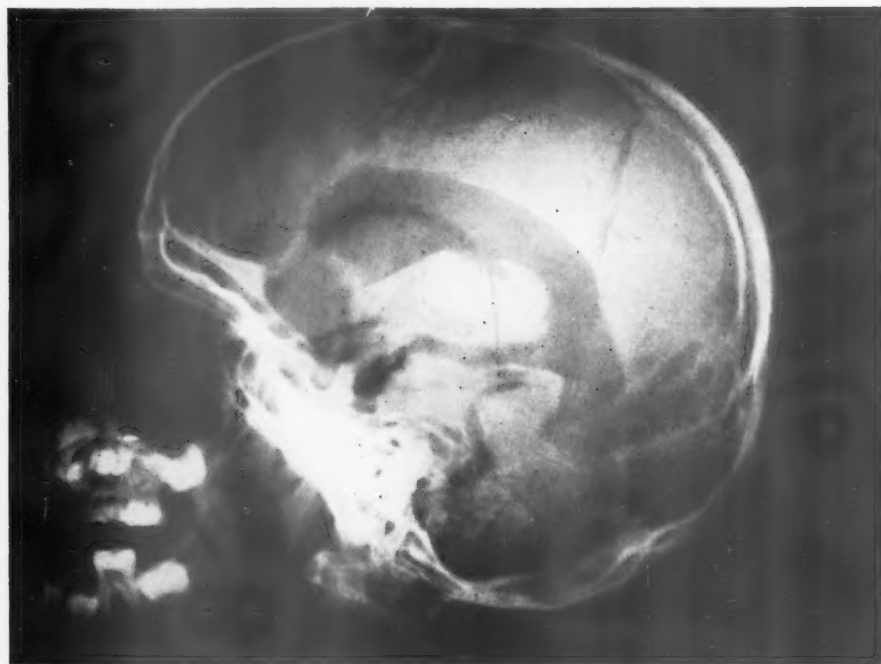


FIG. 11.—J. C. McG., 1935.



FIG. 12.—J. C. McG., 1935.



FIG. 13.—R. C., 1935.



FIG. 14.—A. B., 1935.

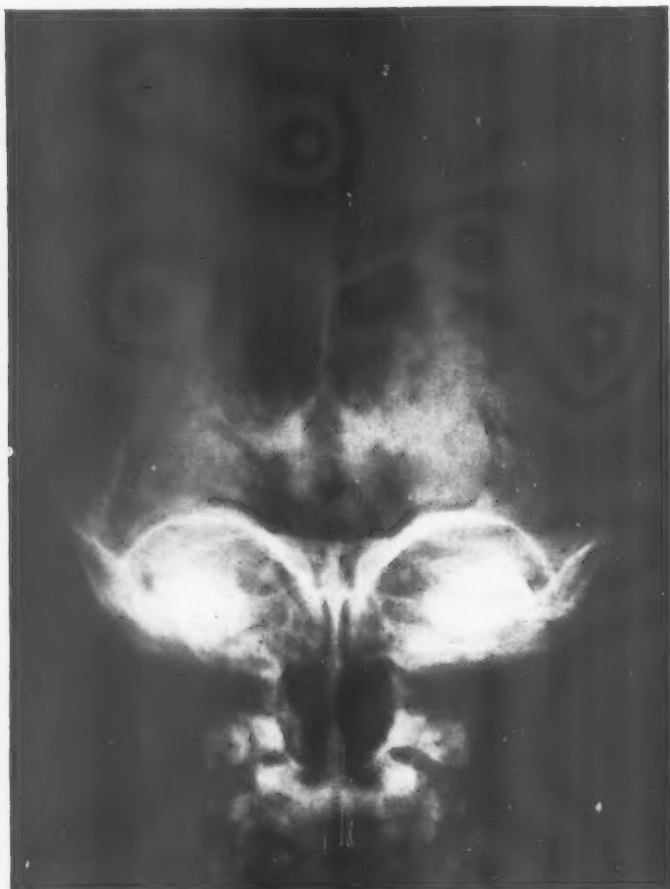


FIG. 15.—A. B., 1935.



FIG. 16.—A. P., 1933.

inkling of the presence of gross deficiency in cerebral bulk was gained from the amount of cerebrospinal fluid removed during the procedure; in one case (A. A., 1933) this was 260 c.c. In general, the lesions disclosed by encephalography were the following: hydrocephalus, either compensating or communicating; dilatation of the basal cisterns; cortical atrophy; and occasionally areas suggestive of arachnoiditis over the cerebral hemispheres. An example which includes all these lesions is seen in fig. 14 and 15 (A. B., 1935). The dilated intracerebral ventricular system is well outlined, and the large size of the cisterna interpeduncularis is a striking feature. Over one hemisphere the cortical air channels are poorly outlined, and on this side the ventricle is slightly larger than on the other, suggesting a greater loss of cortical substance. In fig. 16 (A. P., 1933) a more marked loss of cortical tissue is to be seen, the convolutions standing out as radiating tongues of solid tissue. In fig. 17 and 18 (E. M. S., 1936) widespread convolitional atrophy is apparent, and this involves the parieto-occipital area as well as the frontal. The ventricles are dilated, but the basal cisterns are not proportionately enlarged: it is believed that this combination of findings indicates a primary failure of development of the cortex, and the clinical history of the case supports this view, for the child had not developed either intellectually or physically from the time of birth. A somewhat bizarre appearance is seen in fig. 19 and 20 (C. G., 1935), in which an extreme dilatation of the occipital horn of the lateral ventricles is present, together with dilatation of the third ventricle, while the frontal horns of the lateral ventricles are relatively normal. The authors cannot offer any explanation for these appearances. Fig. 21 (A. A., 1933) represents an extreme degree of lack of cerebral tissue; it would appear that the greater part of one hemisphere is absent, although the faint outlining of the corresponding lateral ventricle suggests that at least a rim of cerebral tissue remained. It is believed that the appearances indicate a primary agenesis. Although the child could walk, clinical examination revealed the signs of an extensive upper motor neuron lesion corresponding to the side of the cerebral defect, and an extreme degree of intellectual impairment was present. Fig. 22 (U. T., 1935) is the encephalogram of a case of progressive mental deficiency. Cortical air markings are absent, and in this regard it is of great interest that six years previously the patient had for some days exhibited the symptoms of meningeal irritation. The procedure was followed by so marked an improvement in his intelligence that it was repeated, with a further improvement, after an interval of a year.

GROUP 4. MISCELLANEOUS.

Seven cases have been included in the miscellaneous group. The reasons for admission will be found in table 4 (p. 124). The case of 'coal gas poisoning' proved to be an emaciated mental defective with quadriplegia,

CASE	SEX	AGE	REASON FOR ADMISSION	NATAL HISTORY		BEGAN TO		AGE OF ONSET PRESENT STATE	PHYSICAL EXAM.	NEUROLOGICAL EXAM.
				NO. IN FAMILY AND PLACE	LABOUR	WALK	TALK			
A.P. 1933	F.	11 m.	Fits ? amentia	2/2	—	—	—	6 wk.	Hydroceph. Head 18 in.	No control over neck
M.D. 1933	F.	5 yr.	Cannot speak	5/5	Rapid	2 yr.	—	—	Anaemia	—
A.A. 1933	M.	4 yr. 6 m.	Amentia	1/1	—	4 yr.	2 yr.	—	Wasted. Head 18 in.	Rt. plantar extensor
O.T. 1934	F.	9 m.	Amentia	3/3	—	—	—	3½ m.	—	Frequent squinting, hypotonic
U.T. 1934 U.T. 1935	M.	11 yr. 12 yr.	Becoming duller at school	6/6	—	11 m.	1 yr.	6 yr.	—	—
M.G.E. 1935	F.	6 yr.	Defective speech	3/3	—	2 yr.	? 5 yr.	—	Micro- cephalic type of head	—
A.B. 1935	M.	2 yr. 6 m.	Takes no notice	3/3	—	—	—	—	Head 17 in. Micro- cephalic. Weighs 28 lb.	—
G.A.S. 1935	M.	3 yr.	Dull. Fainting attacks	1/1	Premature 1 mth.	1 yr. 6 m.	1 yr.	—	Head 19½ in. Wasted 24 lb.	Left plantar extensor K.J. + +
C.G. 1935	M.	1 yr. 4 m.	Backward	4/4	—	—	—	—	Toneless	—
E.M.S. 1936	F.	1 yr. 3 m.	Wasting. Too quiet	3/3	Very rapid. Cord round neck	—	—	From birth	14 lb.	Flexibilitas cerea
J.H.W. 1936	F.	7 yr.	For report ? Mental defect	9/7	—	9 m.	11 m.	—	—	K.J. + + [Intelligent child— with rather slow cerebration]
M.B. 1936	F.	3 yr.	? Mental defect	2/2	Very rapid	1 yr. 9 m.	—	—	28 lb.	Movements are rather choreic
C.B. 1936	F.	6 yr.	Cannot speak	3/1	—	4 yr.	Says Mama	? 3 m.	Micro- cephalic type of head	Persistent insomnia. Restless and noisy
V.S. 1936	F.	3 yr.	Backward	4/4	—	1 yr. 2 m.	—	—	—	—
I.M. 1933	M.	10 m.	Amentia with fits	2/2	Rapid	1 yr.	1 yr.	? Birth	—	—
G.G.C. 1935	M.	10 m.	Amentia with fits	4/4	Difficult	—	—	3 wk.	Head 16 in. with temporal recession	Quadriplegia
G.B. 1936	M.	11 yr. 3 m.	Amentia with fits	2/1	Premature rapid	4 yr. 6 m.	4 yr. 6 m.	Birth	Head 19 in.	—

LE 3.

MENTAL DEFECT.

OPHTHAL. EXAM.	MENTAL DEFECT	CONVULSIONS		C.S.F. REMOVED C.C.	FINAL DIAGNOSIS	ENCEPHALOGRAM AND REMARKS
		AGE AT ONSET	NATURE G=GENERAL L=LOCAL			
—	Yes slight	6 wk.	G.	120	Hydrocephalus with amentia	Internal hydrocephalus Cortical atrophy
—	Yes	6 wk.	G.	95	Amentia	Mild hydrocephalus Marked cortical atrophy
Double optic atrophy	Yes	4 m.	L. Right. seldom G. numerous minor	260	Primary cerebral defect	Almost complete absence of cortical tissue on left side. Both ventricles grossly dilated
—	Yes	—	—	84	Amentia	Well marked cortical atrophy. Will probably have slowly progressive hydrocephalus
—	Yes	—	—	70	Amentia (secondary)	Communicating hydrocephalus from arachnoiditis involving cortical path- ways Had meningitis at 6, during measles. Hearing improved; brighter
—	Slight	—	—	63	Amentia	Considerable cortical atrophy at vertex (R.) corresponding to upper end of Rolando's fissure
—	Yes (noisy)	—	G. (minor)	56	Amentia	Basal cisterns somewhat dilated Communicating hydrocephalus with mark- ed dilatation of ventricles and basal cisterns Much quieter after enceph.
—	Yes	—	G. (minor)	133	Amentia	Hydrocephalus, grave, 3/4, with widening of sub-arachnoid spaces. Primary developmental defect
—	Yes	—	—	55	Amentia	Marked bilateral dilatation of occipital horns of lateral ventricles. Frontal horns normal. Third ventricle dilated, fourth ventricle normal. Subarachnoid path- ways normal
—	Yes	—	—	170	Amentia	Widespread convolutional atrophy with hydrocephalus 2/4. Probably con- genital defect.
—	No	—	None	81	—	Ventricles symmetrically dilated 1/4. No lateral deviation. Cisterns some- what dilated. Poor cortical pathways, especially on Right. ? Some adhesive arachnoiditis
—	Yes	—	—	55	Amentia	Normal
—	Yes	3 m.	G.	79	Amentia	Ventricles enlarged +1, with some slight evidence of cortical atrophy in frontal region Quieter after enceph.
—	Yes	—	—	26	Amentia	Encephalogram abandoned because of difficulty with anaesthetic
—	Yes	2 days	G.	60	Amentia	Ventriculogram—Normal Cortical atrophy with associated hydro- cephalus
—	Complete amentia	3 wk.	G.	80	Amentia	Marked internal hydrocephalus and cortical atrophy especially on left side
—	Imbecile	1 day	G.	76	Amentia	Absence of subarachnoid markings

who was sent to hospital for resuscitation after an attempt to murder him. The encephalograms (fig. 23 and 24) (E. C., 1933), show advanced loss of cortical substance with compensatory hydrocephalus. Except in one area convolutional arrangement is lacking, and the hemispheres, or what is left of them, appear as smooth masses. This child was prematurely born; paralysis was first noted in the face one week after his birth. Some weeks after encephalography this patient died from septicaemia arising from an otitis media, and the encephalographic diagnosis was fully confirmed at autopsy. One of the most interesting encephalograms in the series was obtained in a case of syphilitic meningitis (S. R., 1935). The appearances are shown in fig. 25 and 26. It will be noted that a communicating hydrocephalus of an extreme degree is present; but the most important feature is the punctuate distribution of the air over the hemispheres. These rounded areas were interpreted as areas of localized cortical atrophy, resulting from nutritional disturbances secondary to vascular obliterative disease. The encephalograms in fig. 27 and 28 (J. W., 1935) were obtained from a patient admitted for the first time nine months previously on account of wasting. After making a good recovery, his temperature suddenly fell to 89° F. (rectal), and for one week thereafter he had a succession of generalized and severe convulsions. The encephalograms show an extreme and unsuspected degree of cerebral atrophy with compensatory hydrocephalus, and in this case also there is an almost complete absence of arrangement of cortical tissue in convolutions. Presumably the condition represents a primary cerebral defect, although curiously enough, his convulsions have been limited to the week following the attack of hypothermia. The details of the remaining cases are of less interest and may be found in table 4.

General discussion.

After a certain number of encephalograms had been obtained in this series, it was naturally asked whether the procedure was a justifiable one, and in the best interests of the patients. It is not to the point that the test is a simple one, with little or no risk attached to it; the question really is, whether or not from it useful or even essential information can be obtained, to supplement the findings on clinical examination. It was decided, upon consideration, that not only was the procedure often well worth while, but that there were grounds for including it as a routine test in the types of patient investigated.

The evidence for and against this view may now be collected, and it is perhaps fairer to state at the outset that encephalography, at least in the present series, has not helped by disclosing lesions that might be rectified by



FIG. 17.—E. M. S., 1936.



FIG. 18.—E. M. S., 1936.

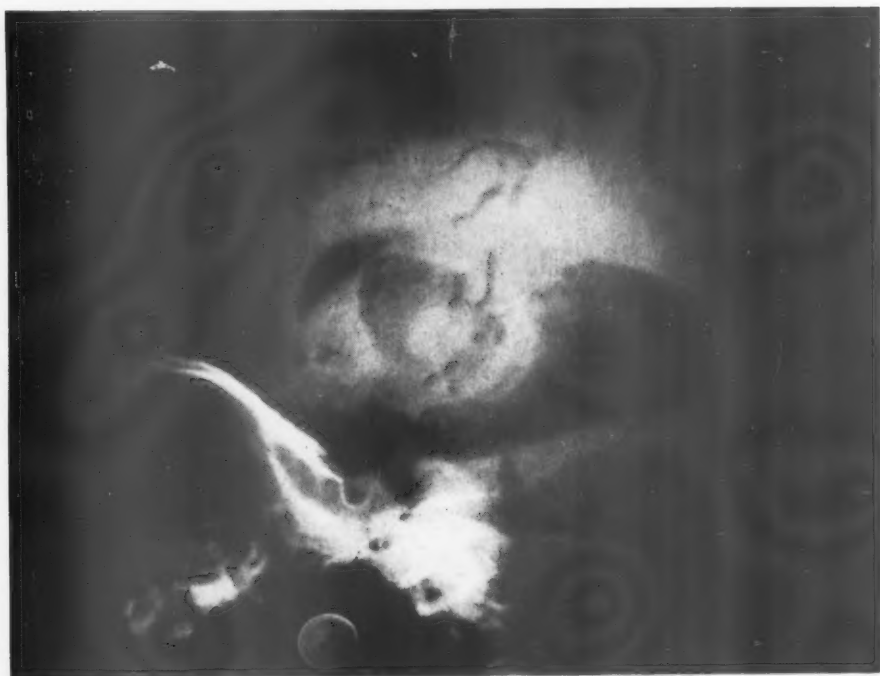


FIG. 19.—C. G., 1935.



FIG. 20.—C. G., 1935.



FIG. 21.—A. A., 1933.



FIG. 22.—U. T., 1935.



FIG. 23.—E. C., 1933.



FIG. 24.—E. C., 1933.

therapeutic measures either medical or surgical. This is disappointing, but not wholly unexpected, for at least the surgical treatment of these convulsive states in children has been almost completely abandoned as ineffective, after a trial of numerous and varied operations; and with this conservative surgical attitude the authors were, and still are, in complete agreement. The rarity of tumours of the hemispheres in childhood is well recognized, and almost the only indication for surgical interference would be the discovery of a supratentorial growth, clinical signs of which were scanty or lacking. However, the procedure may supply information which may be of diagnostic or prognostic value, or both. The neurological examination in most cases of so-called 'idiopathic epilepsy,' and in cases of mental defect, is notoriously negative, and gives little or no information regarding the extent of the cerebral damage. This information is readily obtained by encephalography, and it appears to be of considerable importance. Thus it enables the physician to explain to the parents of the child that an actual lack of brain substance is present. If the procedure is carried out early, this will often permit of arrangements being made for the custody and care of children, either because institutional treatment is essential for hygienic reasons, or because such mental powers as the child possesses, or is likely to possess, are best developed under expert care.

When cerebral defects are revealed they have been frequently a surprise, and their extent has been unexpected. Although it is believed that the results of clinical examination should be given much weight, it will have been realized that without the additional information afforded by encephalography a line of treatment would have been advised that was foredoomed to failure. The clinician is often inclined to advise a prolonged course of treatment, in the hope that the patient may belong to the fairly numerous group in which mental and physical development, though long delayed, ultimately become at least adequate for adult economic self-sufficiency. Moreover, random inspection of the encephalograms of even a small series of 'epileptics' will cure even the most ardent advocate of adherence to a uniform method of treatment.

In a certain proportion of epileptics the encephalograms are normal, and it is a decided limitation of the usefulness of the test that this does not depend on the mildness of the symptoms, either as regards severity or frequency of convulsive attacks. Again it will be apparent from the tables of case records that a demonstrably large cerebral defect is not necessarily associated with the presence of convulsions, either generalized or localized. These limitations are, however, more apparent than real, for the clinical history in cases of this type naturally supplies the missing information; although of necessity in retrospect.

Finally, it must be strongly emphasised that in the investigation of cerebral conditions of these types, encephalography is on no account to be used as a diagnostic shortcut. The advice finally given to the child's parents

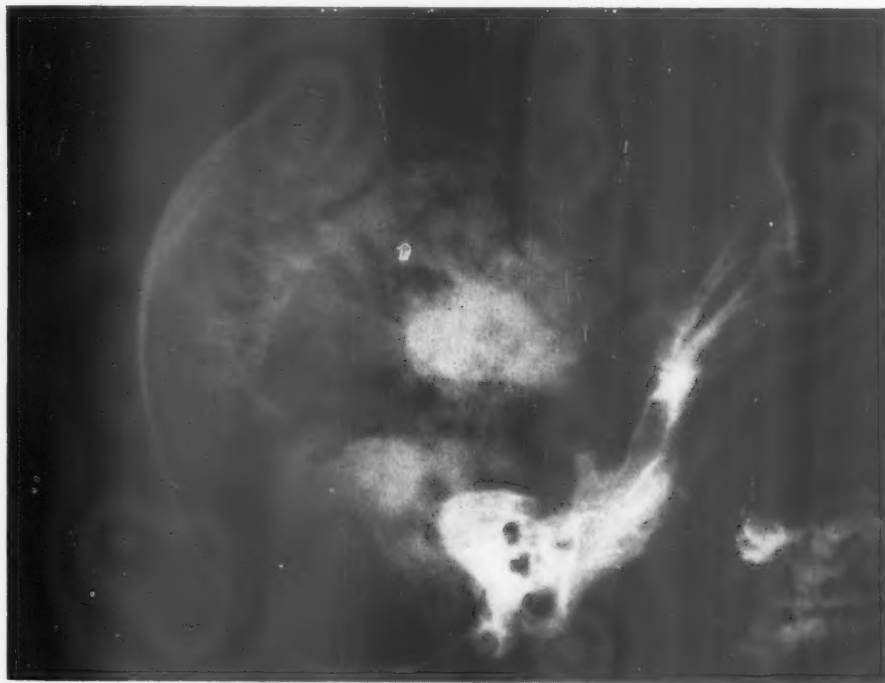


FIG. 25.—S. R., 1935.



FIG. 26.—S. R., 1935.



FIG. 27.—J. W., 1935.



FIG. 28.—J. W., 1935.

TAB

GROUP 4.

CASE	SEX	AGE	REASON FOR ADMISSION	NATAL HISTORY		BEGAN TO		AGE OF ONSET PRESENT STATE	PHYSICAL EXAM.	NEUROLOGICAL EXAM.
				NO. IN FAMILY AND PLACE	LABOUR	WALK	TALK			
E.C. 1933	M.	8 yr.	Coal gas poisoning	2/2	Premature 3½ lb.	—	—	1 wk.	Emaciated. Cannot chew. Projectile vomiting attacks	Quadriplegia
E.D. 1935	M.	3 yr. 9 m.	Spastic hemiplegia	4/3	Hyper- emesis	Late	Late	8 m.	Head 22½ in. was large at birth	Rt. arm and leg spastic
P.P.F. 1935	M.	5 yr. 6 m.	Pain in head after a fall	8/7	—	1 yr.	1 yr.	4 yr. 6 m.	—	—
S.R. 1935	F.	7 yr.	? Amentia	3/2	—	10 m.	1 yr.	? 4 yr.	—	Ataxic. Plantars extensor. Reflexes all + co-ordination impaired
J.W. 1935	M.	1 yr. 1 m.	? Blind	1/1	—	—	—	4½ m.	Head 17 in. Small A.P. diam.	—
W.D.M. 1936	M.	4 yr.	Lost power of speech and hearing	3/3	Rapid	11 m.	10 m.	2 yr. 6 m.	—	Healed labyrinthitis both sides
J.R. 1935	F.	4 yr.	Spastic hemiplegia with fits	7/4	—	2 yr.	1 yr. 6 m.	? 1 yr.	—	Right hemiplegia improving
J.R. 1936	F.	4 yr. 6 m.	For repeat enceph.	—	—	—	—	—	—	—

LE 4.

MISCELLANEOUS.

OPHTAL. EXAM.	MENTAL DEFECT	CONVULSIONS		C.S.F. REMOVED C.C.	FINAL DIAGNOSIS	ENCEPHALOGRAM AND REMARKS
		AGE AT ONSET	NATURE G=GENERAL L=LOCAL			
—	Imbecile	—	—	321	Amentia	Advanced bilateral cortical atrophy with compensatory hydrocephalus. [P.M.]
—	Yes	8 m.	L. Right ceased at 3 yr.	110	Congenital hydrocephalus	Widespread cortical atrophy. Ventricles not outlined Ventriculogram later showed huge bilateral hydrocephalus, gross reduction of cortex Block in absorbing mechanism. [P.M.]
—	—	—	—	45	—	Normal
Dises rather pale	Yes (lately)	4 yr.	G. only one recorded	110	Congenital syphilis	Marked bilateral dilatation of lateral ventricles. Gross enlargement of basal cisterns. Widespread cortical atrophy (See text) W.R.: C.S.F. + + + +
Optic atrophy	Yes	4½ m.	G. For 7 days only. None since	50	Not determined	Extreme degree of cortical atrophy, especially on right. Little or no differentiation into convolutions. Compensatory dilatation of lateral ventricles
—	—	—	—	71	Chronic meningitis	Basal cisterns dilated +1 +2. Sub-arachnoid markings not well seen. Mild interference with absorption of C.S.F. Probably had a meningitis at 2½ yr.
—	—	1 yr.	G.	45	Spastic hemiplegia	Practically all air is trapped in basal cisterns. Ventricles not outlined. A few pathways on both frontal lobes and some air between hemispheres and falx cerebri 2nd Enceph. Same findings Ventriculogram later—Normal
				50 (60 air)		

will be based upon an exhaustive clinical examination, the encephalographic findings, and a knowledge of the environment, social and personal, of the patient.

Summary.

1. A technique of encephalography is described (see part I).
2. A series of forty-seven cases is presented, in which encephalography has been used as an additional method of investigation.
3. The principal forms of cerebral defect encountered in the investigation are illustrated and described.
4. Reasons are adduced for the opinion that the method is of value in diagnosis, in prognosis, and occasionally in treatment.

THE THERAPEUTIC VALUE OF VITAMINS A & D IN MEASLES

BY

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Objects of investigation.

The investigation described in this communication was planned with two main objects in view; first, to determine whether the administration of vitamin D, or of vitamins D and A, to children with measles had any favourable influence on the course of the disease; and secondly, to determine whether vitamin A would lessen the incidence of the minor skin infections common in measles. J. B. Ellison's work¹ on measles at the Grove Hospital in London suggested that the combined administration of vitamins D and A lessened the mortality, but there was the apparently discrepant finding that the incidence of otorrhoea in his cases was not favourably affected. So far as the present authors are aware, no series of cases has yet been published in which the therapeutic value of these vitamins has been satisfactorily established for an already existant acute infection. On the other hand, there is much to indicate that resistance to infections is reduced in children suffering from an overt deficiency of either of these vitamins². Hence it seemed that Ellison's tentative findings, as he himself said, required corroboration. A previous investigation undertaken by Mackay³ suggested that the earliest evidence of vitamin A deficiency in infants might be an increased susceptibility to skin infections, and a study of the literature reveals that such infections are common with overt vitamin A deficiency⁴. In measles, infections of the skin and mucuous membranes are common. It was, therefore, hoped that if some of the children suffered from a deficiency of vitamin A, the addition of this substance to their diet would diminish the number of such infections, and provide corroborative evidence of the findings with infants.

Clinical material and scheme of investigation.

The present investigation was carried out at the North Eastern Hospital, London, between January and July, 1934. The children admitted were for the most part from families sending their children to London County Council schools, that is they belonged to lower middle class and labouring

class families. The children were of a similar social type to those dealt with by Ellison.

The total number of cases was 713; of these sixteen were subsequently excluded because they were under observation for less than seven days, having been transferred to other wards with another infection, such as whooping cough, diphtheria, chicken pox and enteritis, leaving 697 included in the investigation. The ages varied from two months up to twelve years: 365 were boys and 332 girls.

The children were divided into three groups. All were given the routine diet customary in the hospital. The first group served as controls and received no extra vitamin medication; the second group were given a vitamin D supplement, the third a supplement of vitamin D and vitamin A combined.

The children were under the care of three medical officers. During the first few weeks of the observation M. M., and for the remainder of the time H. L. and M. W. had charge of the children and kept the clinical records on an agreed scheme, an effort being made to co-ordinate findings. When, for example, there was uncertainty as to a diagnosis, M. M. and H. M. M. usually also examined the cases, with the object of arriving at findings which were generally agreed. Five wards were allocated to the children under investigation; three wards being under the charge of H. L. and two under that of M. W. Cases admitted into each ward were included in rotation in each of the three groups. By this means it was hoped to ensure that in each ward and under each medical officer there should be equal numbers of each of the groups, so that the results might not be complicated by differences in ward technique. During the course of the observation, when the number of children had reached about 300, it was found that the groups were not evenly balanced as regards age and presence of pneumonia on admission. In order to rectify this a notice was thenceforward put up in the admission room at the beginning of each week requesting, for example, that the next two children aged one year admitted with pneumonia should be placed in group X, or the next four children aged two years should go into group Y, etc. Apart from this modification the scheme of allocation to the three groups in rotation was continued.

The tabulation of records was carried out by H. M. M. M., with the help of Miss Lorel Goodfellow. Since one person tabulated the findings in all cases this should ensure uniformity of standard in this section of the work.

Diet in hospital and vitamin supplements.

The children during the pyrexial stage of the illness were fed chiefly on milk or milk and cereal. When convalescent the older children received fish or meat and green vegetables at dinner, with a total of one pint of milk and one ounce of butter daily. Unless specially ordered no eggs were given to any children under seven years old and no raw fruit was officially included in the dietary although some fruit was sent in by the parents. The vitamin supplements were prepared and standardized by the British Drug Houses Ltd. The vitamin D group received 3,000

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international units in the form of calciferol daily. This is the nominal equivalent in international vitamin D units of, say, one ounce of cod-liver oil daily; or, what is perhaps more relevant, it is enough to produce in a child healing of active rickets at what would appear to be the maximum rates⁵. The D plus A group received the same amount of vitamin D, and, in addition, the vitamin A equivalent of six drachms of cod-liver oil of 7·5 blue value daily. The vitamins were incorporated in an emulsion made with carrageen and acacia.

Results.

Total fatality rate.—The total number of fatal cases is small (33 deaths among 697 cases; a fatality rate of 4·7 per cent.), and this must be borne in mind in relation to the fact that the case mortality in the three groups is fairly close. Among controls it is 4·3 per cent.; among D cases 4·1 per cent.; and among D plus A cases 5·9 per cent. (see table 1). Thus

TABLE 1.
DEATHS: ALL CAUSES.

	CONTROLS.			D CASES.			D + A CASES.			ALL GROUPS COMBINED		
	NO. OF CASES	DEATHS	CAUSE OF DEATH	NO. OF CASES	DEATHS	CAUSE OF DEATH	NO. OF CASES	DEATHS	CAUSE OF DEATH	NO. OF CASES	DEATHS	DEATHS PER 100 CASES
UNDER 1 YEAR	26	1	P. 1	26	5	P. 3, Ent. 2	25	2	P. 2	77	8	10.4
1 YEAR OLD ...	69	6	P. 5, Enc. 1	69	4	P. 3, S. 1	67	10	P. 10	205	20	9.8
2 YEARS ...	63	1	P. 1	62	1	P. 1	61	0	—	186	2	1.1
3 " ...	33	1	P. 1	33	0	—	28	1	P. 1	94	2	2.1
4 " ...	22	0	—	25	0	—	17	0	—	64	0	—
5 " ...	11	1	P. 1	15	0	—	13	0	—	39	1	2.6
6 YEARS AND OVER	10	0	—	11	0	—	11	0	—	32	0	—
TOTAL ...	234	10	P. 9, Enc. 1	241	10	P. 7 Ent. 1, S. 1	222	13	P. 13	697	33	4.7
FATALITY PER 100 CASES ...	4.3			4.1			5.9			4.7		
DEATHS OCCURRING AFTER 7 DAYS IN HOSPITAL: NO. ...	6			6			7			19		
FATALITY PER 100 CASES ...	2.6			2.5			3.2			2.7		

P. = pneumonia; Enc. = encephalitis; Ent. = enteritis; S. = septicaemia.

the first two groups have all but the same fatality rate, and the D plus A cases a slightly higher rate. If all children dying within one week of admission are omitted, i.e., if only those are considered who had seven days treatment and upwards the comparative results are similar: the fatality rates being 2.6 per cent., 2.5 per cent. and 3.2 per cent. respectively. Again there is no evidence of any favourable effect on the fatality rate from the vitamin administration.

Analysis of fatality rates in the three groups.—It is obviously necessary to examine whether the groups were evenly matched on admission before judgment can be passed on the deductions drawn. It is well known that the fatality rate from measles varies widely with age: if the three groups are combined it is found that of those under two years old 9.9 per cent. died, of those two and three years old 1.4 per cent. died, and of those of four years and over only 0.7 per cent. died (see table 1). Table 1 and table 2, however, show that the number of children in each age division was similar in the three groups, hence the results are not vitiated by discrepancies in age between the three groups.

TABLE 2.

AGE: DISTRIBUTION OF CASES.

	CONTROLS		D CASES		D + A CASES		ALL GROUPS COMBINED	
	NO.	PER CENT.	NO.	PER CENT.	NO.	PER CENT.	NO.	PER CENT.
UNDER 2 YR.	95	41	95	39	92	41	282	40
2 & 3 YR. OLD	96	41	95	39	89	40	280	40
4 YR. & UPWARDS	43	18	51	21	41	18	135	19
	234		241		222		697	

Another obvious factor influencing the fatality rate is the incidence of pneumonia at the time of admission. Of the total number of deaths (i.e., 33) 29 (or 88 per cent.), were due to pneumonia, and of these 29 children 25 had pneumonia on admission (which accounts for 76 per cent. of the total 33 deaths), and four developed pneumonia after admission. Of the remaining four deaths, two were due to enteritis, one to septicaemia and one to encephalitis, these complications developing after admission. As already stated, the attempt was made to allocate equal numbers of children with pneumonia on admission to each group. The distribution of cases is shown in tables 3 and 4. Considering each group as a whole, the incidence of pneumonia on admission is similar:—controls 13.2 per cent.; D cases 12.0 per cent.; D plus A cases 12.6 per cent.; and the distribution of pneumonia among children of different ages is fairly even between the three groups. This is more easily seen in table 4, where it is shown that among children aged less than two years, and in those aged two years and three years, the incidence of pneumonia on admission is almost identical in the three groups; and of the 33 deaths, 32 were in these age periods.

TABLE 3.
FATALITY AND PNEUMONIA INCIDENCE ANALYSED.

	CONTROLS			D CASES			D + A CASES			ALL GROUPS COMBINED		
	PNEUMONIA ON AFTER ADMISSION		TOTAL DEATHS ALL CAUSES	PNEUMONIA ON AFTER ADMISSION		TOTAL DEATHS ALL CAUSES	PNEUMONIA ON AFTER ADMISSION		TOTAL DEATHS ALL CAUSES	PNEUMONIA ON AFTER ADMISSION		TOTAL DEATHS ALL CAUSES
	No.	Died	No. Died	No.	Died	No. Died	No.	Died	No. Died	No.	Died	No. Died
UNDER 1 YEAR ...	2	1	1	—	1	5	3	1	1	1	1	2
1 YEAR OLD ...	15	5	7	—	6	11	3	1	—	4	14	7
2 " ...	7	1	1	—	1	9	1	1	—	1	7	—
3 " ...	3	1	2	—	1	1	—	—	—	—	4	1
4 " ...	2	—	—	—	—	1	—	—	—	—	—	—
5 " ...	1	1	1	—	1	1	—	—	—	—	2	1
6 YEARS AND OVER ...	1	—	1	—	—	1	—	—	—	—	2	—
TOTALS ...	31	9	13	—	10	29	7	4	—	10	28	9
PER CENT. OF TOTAL CASES ...	13.2	3.8	5.6	—	4.3	12.0	2.9	1.7	—	4.1	12.6	4.1
TOTAL NO. OF CASES OF PNEUMONIA.	No. died		No. per cent. died		No. died		No. per cent. died		No. died		No. per cent. died	
	44		20.5		33		21.2		40		32.5	
TOTAL NO. OF CASES OF PNEUMONIA.	No. died		No. per cent. died		No. died		No. per cent. died		No. died		No. per cent. died	
	29		24.8		13		32.5		117		24.8	
TOTAL NO. OF CASES OF PNEUMONIA.	No. died		No. per cent. died		No. died		No. per cent. died		No. died		No. per cent. died	
	29		24.8		13		32.5		117		24.8	

TABLE 4.

AGE—DISTRIBUTION OF CASES OF PNEUMONIA ON ADMISSION.

	CONTROLS		D CASES		D + A CASES	
	NO. OF CASES	PNEUMONIAS No. PER CENT.	NO. OF CASES	PNEUMONIAS No. PER CENT.	NO. OF CASES	PNEUMONIAS No. PER CENT.
UNDER 2 YR.	95	17 18	95	16 17	92	17 18
2 & 3 YR. OLD	96	10 10	95	10 11	89	11 12
4 YR. & UPWARDS	43	4 9	51	3 6	41	0 0
		31		29		28

In these cases the fatality rate varied appreciably according to the season of the year during which they were admitted. Thus there were 27 deaths among 426 cases admitted in January to April, a fatality of 6·3 per cent.; whereas among 271 cases admitted in May to July there were only six deaths, a fatality of 2·2 per cent. Table 5 shows that though the percentage of each group admitted in the months January to April did not differ widely, a slightly larger proportion of D plus A cases was admitted in these more unfavourable months. However, the fatality figures in table 5 show that if cases admitted during either January to April, or May to July, are separately compared, there is still no evidence of advantage from vitamin administration.

TABLE 5.

SEASON OF ADMISSION: DISTRIBUTION OF CASES AND FATALITY.

	JANUARY—APRIL				MAY—JULY			
	CASES		DEATHS		CASES		DEATHS	
	NO.	PER CENT.	NO.	PER CENT.	NO.	PER CENT.	NO.	PER CENT.
CONTROLS	137	58·5	7	5·1	97	41·5	3	3·1
D CASES	147	61·0	10	6·8	94	39·0	0	0·0
D + A CASES	142	64·0	10	7·0	80	36·0	3	3·8

TABLE 6.

FATALITY RATES IN RELATION TO THE STAGE OF THE ILLNESS ON ADMISSION.

STAGE OF DISEASE ON ADMISSION :	1ST DAY OF RASH	2ND DAY OF RASH	3RD DAY & LATER	BEFORE RASH	DEVELOPED IN HOSPITAL	MEASLES
A. ALL CASES.						
NO. OF CASES	350	203	114	28		2
NO. DIED	10	8	13	2		—
PER CENT. DIED	2·9	3·9	11·4	7·1		—
			10·6			
B. CASES UNDER 2 YR. OLD.						
NO. OF CASES	6·5	79	51	11		2
NO. DIED	9	8	9	2		—
PER CENT. DIED	139	10·1	17·6	18·2		—
			17·7			

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A relation also exists between the stage of the disease at which children were admitted and the fatality rate. The fatality rates according to the stage of the disease on admission are shown in table 6. The lowest fatality is shown by the cases admitted on the day the rash came out; it is higher for those admitted on the second day of the rash; and highest for children admitted either earlier or later than these dates. Probably these figures indicate that cases coming in before the rash developed, or after the rash had been out for two days, tended to be children who were sent in because they were seriously ill. If the distribution of cases among the three groups is examined according to the stage of the disease on admission, it is found that the D plus A group was at a distinct disadvantage because a considerably larger proportion of the young children in this group were admitted either before the appearance of the rash or on or after the third day of the rash (table 7). Hence it is probable that the D plus A group contained a

TABLE 7.
STAGE OF THE ILLNESS ON ADMISSION : DISTRIBUTION OF CASES.

	CONTROLS.		D CASES.		D + A CASES.	
	No.	PER CENT. OF TOTAL	No.	PER CENT. OF TOTAL	No.	PER CENT. OF TOTAL
ALL CASES.						
DEVELOPED MEASLES IN HOSPITAL	2	0.9	—	—	—	—
ADMITTED BEFORE RASH ...	8	3.4	7	2.9	13	5.9
„ 3RD DAY OF RASH AND LATER ...	38	16.2	36	14.9	40	18.0
„ 1ST DAY OF RASH ...	118	50.4	133	55.2	99	44.6
„ 2ND DAY OF RASH ...	68	29.1	65	27.0	70	31.5
CASES UNDER 2 YEARS OLD.						
DEVELOPED MEASLES IN HOSPITAL	2	0.9	—	—	—	—
ADMITTED BEFORE RASH OR 3RD DAY AND LATER ...	15	6.4	18	7.5	29	13.2
„ 1ST DAY OF RASH ...	48	20.5	56	23.2	35	15.8
„ 2ND DAY OF RASH ...	30	12.8	21	8.7	28	12.6

TABLE 8.
SEX : DISTRIBUTION OF CASES.

		CONTROLS		D CASES		D + A CASES	
		No.	PER CENT.	No.	PER CENT.	No.	PER CENT.
MALES	...	124	53	119	49	122	55
FEMALES	...	110	47	122	51	100	45

larger proportion of children under two years old who were seriously ill on admission, and that this factor contributed to the higher fatality rate among them.

One more factor requiring consideration is the sex distribution since the fatality rate was higher among boys than among girls. There were 365 males, of whom 20 or 5.5 per cent., died; and 332 females, of whom 13, or 3.9 per cent., died. As shown in table 8, the distribution of males and females was dissimilar in the three groups, and again the D plus A group was at a small disadvantage: the D group contained 49 per cent. males, the controls 53 per cent., and the D plus A group 55 per cent.

It so chanced, therefore, that the D plus A group was at a disadvantage in the sex and seasonal distribution of cases, and in the stage of the disease at which the children were admitted, and the D group on the other hand was more favourably placed than the other two groups as regards sex distribution and stage of admission. This may explain the higher fatality rate among the D plus A cases, but these differences were not sufficiently great in themselves to wipe out a favourable influence of treatment with vitamin A and D on the fatality rate, had any such occurred.

Incidence of pneumonia after admission.—Even though treatment with these vitamins did nothing to prevent death (and the majority of deaths were from pneumonia already present on admission) it might have had a favourable effect in diminishing complications occurring after admission. As regards pneumonia, its incidence after admission was similar among controls and D plus A cases, but it was considerably lower in the D group (see table 9). Thus vitamin A administration did not lessen this complica-

TABLE 9.

PNEUMONIA DEVELOPING AFTER ADMISSION.

	CONTROLS		D CASES		D + A CASES	
	NO. OF CHILDREN WITHOUT PNEUMONIA ON ADMISSION	NO. WHO DEVELOPED PNEUMONIA	NO. OF CHILDREN WITHOUT PNEUMONIA ON ADMISSION	NO. WHO DEVELOPED PNEUMONIA	NO. OF CHILDREN WITHOUT PNEUMONIA ON ADMISSION	NO. WHO DEVELOPED PNEUMONIA
TOTAL	203	13	212	4	194	12
PERCENTAGE		6.4		1.9		6.2

tion. It can only be argued that vitamin D did so if it is supposed that vitamin A in the dosage given had a harmful effect, so wiping out the benefit accruing from vitamin D in the D plus A group, and this on the face of it is most unlikely.

The difference, however, between the controls and D cases is only of 2.12 times its standard error so that the odds against it having arisen merely by chance are not very large.

Incidence of otorrhoea after admission.—One of the medical officers (H. L.) examined the ear drums of all children admitted to three out of the five wards, and found catarrhal or inflammatory changes to be almost as constant a feature in the ear as they were in the conjunctivae. No attempt

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has been made to grade these changes, but the patients have been divided according to whether or not they developed otorrhoea.

On admission the case incidence of otorrhoea was similar in the three groups: controls 3.0 per cent.; D cases 3.7 per cent.; and D plus A cases 3.2 per cent. The total incidence (before and after admission) was greater in the vitamin-treated groups; the figures being, control group 12.4 per cent., D cases 15.8 per cent., and D plus A cases 17.1 per cent. Table 10 shows

TABLE 10.

INCIDENCE OF OTORRHOEA.

	CONTROLS				D CASES				D + A CASES			
	No. OF CHILDREN	No. OF CHILDREN WITH OTORRHOEA			No. OF CHILDREN	No. OF CHILDREN WITH OTORRHOEA			No. OF CHILDREN	No. OF CHILDREN WITH OTORRHOEA		
		ON ADMISSION	AFTER ADMISSION	TOTAL		ON ADMISSION	AFTER ADMISSION	TOTAL		ON ADMISSION	AFTER ADMISSION	TOTAL
TOTAL CASES ...	234	7	22	29	241	9	29	38	222	7	31	38
PER CENT.	3.0	9.4	12.4	...	3.7	12.0	15.8	...	3.2	14.0	17.1
CHILDREN WITH OUTOTORRHOEA ON ADMISSION	227		22		232		29		215		31	
PER CENT.		9.7		...		12.5		...		14.4	

the percentage of children who were admitted without otorrhoea and developed it after admission; the figures are, controls 9.7 per cent., D cases 12.5 per cent., and D plus A cases 14.4 per cent. Again the D plus A group comes out worst. Presumably the factors which have already been noted as placing the D plus A group at a slight disadvantage played their part here also, but these differences in incidence of otorrhoea after admission are not more than might easily have arisen by chance.

Incidence of all complications excluding skin lesions.—An attempt was made to assess the incidence of all complications which developed after admission, and this is set out in table 11. Here the results are less certain, because the dividing line between, for example, changes in the mouth ordinarily occurring in measles and a stomatitis which should be reckoned as a complication is absolutely arbitrary. Even in view of this difficulty, it would be expected that if any marked discrepancy in the incidence of such complications existed between the three groups it would show itself.

Actually the differences are small. In table 11 the incidence of complications is shown as the incidence per 1,000 child-days for complications affecting respectively the eyes, mouth, throat and nose, ears, larynx and bronchi, and lungs, as well as for other complications. The largest difference is for pneumonia which has already been considered. The total incidence of complications occurring after admission per 1,000 child-days is, controls 32.1, D cases 30.1, and D plus A cases 34.8, rates which considering the number of children in each group are remarkably similar and show no advantage

TABLE 11.

INCIDENCE OF COMPLICATIONS WHICH DEVELOPED AFTER ADMISSION.

(Cross infections with other fevers excluded.)

	No. OF CHILD- REN	DAYS OF OBSER- VATION	INFECTIONS AFTER ADMISSION.							TOTAL ATTACKS COM- BINED
			EYES	MOUTH	THROAT AND NOSE	EARS*	LARYNX AND BRONCHI	LUNGS	OTHER INFECTIONS	
CONTROLS.										
No.	234	4451	11	24	30	30	11	13	24	143
ATTACKS PER 1,000	—	—	2.5	5.4	6.7	6.7	2.5	2.9	5.4	32.1
CHILD-DAYS										
D CASES.										
No.	241	4348	9	16	20	40	9	4	33	131
ATTACKS PER 1,000	—	—	2.1	3.7	4.6	9.2	2.1	0.9	7.6	30.1
CHILD-DAYS										
D + A CASES.										
No.	222	4193	12	24	23	45	11	12	19	146
ATTACKS PER 1,000	—	—	2.9	5.7	5.5	10.7	2.6	2.9	4.5	34.8
CHILD-DAYS										
D CASES AND D + A CASES COMBINED.										
No.	463	8541	21	40	43	85	20	16	52	277
ATTACKS PER 1,000	—	—	2.5	4.7	5.0	10.0	2.3	1.9	6.1	32.4
CHILD-DAYS										

* Double otorrhoea has been reckoned as two 'attacks.'

to the vitamin-treated groups. Children admitted on the day of appearance of the rash were separately considered. In practice this is the stage of the disease at which the majority of cases are diagnosed. Again it was found that the incidence of complications after admission was closely similar in the three groups.

Duration of pyrexia after appearance of rash.—If the incidence of secondary infections was higher in one group than in the others, one would expect this to be reflected in an increase in the length of the average pyrexial

period for that group. Table 12 shows the average number of days of pyrexia for each group, counting from the day of the rash. A child coming in with pyrexia on the fourth day from the appearance of the rash and continuing to have a temperature above normal for another three days, would be reckoned as having seven days of pyrexia, though only in hospital for three of those seven days. On the other hand, a child coming in with a normal temperature six days after the appearance of the rash was omitted from the tables because there was no information available as to the duration of the pyrexia. In all eleven patients were omitted. The average number of days of pyrexia after the appearance of the rash was as follows: controls 6.6 days, D cases 6.2 days, and D plus A cases 6.5 days. Hence these figures provide no evidence of any favourable effect on the course of this disease from the vitamins given.

TABLE 12.
DAYS OF PYREXIA AFTER APPEARANCE OF RASH.

	NO. OF CASES	DAYS OF PYREXIA	AVERAGE DAYS OF PYREXIA
CONTROLS	229	1,509	6.6
D CASES	237	1,461	6.2
D + A CASES	221	1,443	6.5

Incidence of skin lesions.—The estimation of skin lesions is again a subjective matter—for there is the constantly recurring problem as to whether the conditions recorded should be reckoned as one lesion or several. A child may develop a boil, this may clear up and subsequently he develops an abscess elsewhere. This would be reckoned as two lesions. On the other hand, if the child had multiple boils at one time this would be reckoned as one lesion. Many other arbitrary distinctions had necessarily to be drawn. But as all analyses were made by one person (H. M. M. M.) it is hoped that the subjective factor did not operate for or against any one group. Table 13 shows the results. The total incidence of skin lesions per 1,000 child-days was, controls 21.34, D cases 22.77, and D plus A cases 20.99. When the larger subdivisions are compared, the incidence of skin lesions in the three groups is again similar. There is nothing to suggest that by giving vitamin A the susceptibility to skin lesions was diminished. An attempt was made to compare the duration of the different types of lesions in the three groups, but the data were inadequate.

Duration of time in hospital.—Children were usually kept in hospital until twelve days from the onset of the illness, or until they were free from all complications of the disease (including lesions of the skin) developed in hospital. Thus if giving the vitamin emulsion had any influence on the severity of complications, or the rate at which they cleared up, this should be reflected in a shortened stay in hospital. Four sets of figures are shown in table 14: (a) the average period in hospital for all cases (this included those who died, and those who were transferred to other wards for one

TABLE 13.
SKIN LESIONS DEVELOPED AFTER ADMISSION.

	CONTROLS		D CASES.		D + A CASES	
	No. OF ATTACKS	No. PER 1,000 CHILD-DAYS	No. OF ATTACKS	No. PER 1,000 CHILD-DAYS	No. OF ATTACKS	No. PER 1,000 CHILD-DAYS
LESIONS OF NAPKIN AREA :						
ERYTHEMA ...	2	0.45	6	1.38	2	0.48
PAPULES ...	22	4.94	21	4.83	21	5.01
ULCERS AND SCABS	9	2.02	13	2.99	9	2.15
EXCORIATION AND PUSTULES ...	6	1.35	6	1.38	6	1.43
NARES : EXCORIATION, ETC. ...	9	2.02	3	0.69	7	1.67
INTERTRIGO OR 'CRACKED EARS'	5	1.12	7	1.61	5	1.19
DERMATITIS, PUSTULES, ULCER- ATION, ETC. ...	11	2.47	11	2.53	8	1.91
BOILS, ABSCESES, SEPTIC FINGERS AND TOES ...	7	1.57	15	3.45	13	3.10
IMPETIGO ...	2	0.45	5	1.15	3	0.72
INFECTED ABRASIONS AND TRAUMATA ...	1	0.22	—	—	1	0.24
PAPULES (NOT NAPKIN AREA) ...	19	4.27	11	2.53	11	2.62
HERPES ...	2	0.45	1	0.23	2	0.48

TABLE 14.
DURATION OF STAY IN HOSPITAL AND DURATION OF OBSERVATION.

	ALL CASES.					CASES WHICH RECOVERED.				
	No. OF CASES.	DAYS IN HOSPITAL.	AVER- AGE.	DAYS OF OBSER- VATION.	AVER- AGE.	No. OF CASES.	DAYS IN HOSPITAL.	AVER- AGE.	DAYS OF OBSER- VATION.	AVER- AGE.
CONTROLS ...	234	5743	24.5	4451	19.0	224	5658	25.3	4344	19.4
D CASES ...	241	5649	23.4	4348	18.0	231	5430	23.5	4195	18.2
D + A CASES	222	5188	23.4	4193	18.9	208*	5062	24.3	4071	19.6

*Table I shows for Group D + A a total of 222 children with 13 deaths, leaving 209 cases. Of these, however, one child developed diphtheria while under observation, was transferred to another ward, and died 16 days after transfer, from pneumonia. Hence the figures for recoveries is shown here as 208.

reason or another and from that time ceased to be included in this observation); (b) the average period of observation for all cases; (c) the average period in hospital of the children who recovered (this provides the best figures for comparison for the purpose of this analysis as the average is not shortened by the inclusion of children dying in the first week); and (d) the average period of observation of the children who recovered. Whichever set of figures is considered the averages are close.

The frequency distributions of days of observation are shown in table 15. There is a suggestion of a deficit of short cases in the controls,

TABLE 15.

FREQUENCY DISTRIBUTIONS OF DAYS OF OBSERVATION.

DAYS OF OBSERVATION	CONTROLS PER CENT.	D CASES PER CENT.	D + A CASES PER CENT.
7 - 14 DAYS ...	46	55	49
15 - 24 „ ...	38	29	31
25 - 34 „ ...	8	11	11
35 DAYS AND OVER	8	5	9

balanced by an excess in the 15-24 day group, but no consistent difference in prolonged cases. Statistically the differences are such as might easily arise by chance. The mean times of observation, as calculated from the frequency distribution, are: controls 19.02 days (standard deviation 10.89); D cases 17.74 days (standard deviation 9.90); and D plus A cases 19.08 days (standard deviation 11.35). The means for the control and for the D plus A groups are almost identical. The means for the control and D groups differ by 1.28 days, which has a standard error of 0.98, and is therefore not more than might be due to chance.

Discussion.

One conclusion emerges from the findings set forth, namely, that neither vitamin D, nor vitamins D plus A combined, as here given, had any favourable influence on the course of measles or on its complications during the period the children were under observation. Such results might indicate that few, if any, of the children suffered from a deficiency of either of these vitamins, that though such a deficiency existed it was without effect on the course of measles, or simply that treatment with the vitamins was begun too late and was of too short duration for any effect to be obvious.

Taking these possibilities in order it may be stated that none of the children suffered from obvious vitamin A deficiency; none, for example, had xerophthalmia, nor skin changes which could be diagnosed as phrynoderma or 'papular dry skin.' No tests were made for night blindness. Hence

there is no proof of vitamin A deficiency among the patients. All the children were examined clinically for evidence of rickets past or present. Three had active rickets as shown by the presence of craniotabes. Of the rest, there were thirty-three cases noted as having rickets or 'probable rickets,' or ' ? old rickets.' In the great majority of these the bony stigmata present were slight, so that the existence of rickets, past or present, was often in doubt, and if the clinical findings, the age of the children, and the season are taken into consideration the proportion with active rickets at the time of admission must have been small. It can, therefore, be concluded that none of the children suffered from overt vitamin A deficiency, and very few from overt vitamin D deficiency at the time of admission. Whether or not they suffered from minor grades of deficiency insufficient to produce obvious clinical changes is an open question.

The second possibility, that deficiencies of these vitamins are without influence on the course of measles, is, on the face of it, improbable. There is much to indicate that a deficiency of either vitamin D or vitamin A will increase susceptibility to some infections^{2, 4} and, if so, a diminished resistance to the complications of measles would certainly be expected.

There are various arguments that can be brought forward in favour of the third possibility, namely, that treatment with vitamins was begun too late and was of too short duration to produce obvious results even had vitamin deficiency been present. If it is assumed that the rash usually appears on the fourth day, then 50 per cent. of the present patients started treatment on the fourth day of the disease, and a further 31 per cent. on or after the fifth day. Moreover, the average period of observation was under twenty days. If this is compared with the time needed to produce an effect in rickets, then the earliest radiographic evidence of healing in an overt case of rickets with optimum treatment generally appears in the third week, and may be delayed until the fourth week. Proof of improved general health may be delayed much longer. If vitamin A deficiency is considered, as revealed by 'papular dry skin,' in the only overt case heretofore under the personal observation of one of us, no improvement in the skin condition was apparent until approximately two weeks after treatment with vitamin A was begun⁶.

Thus though the results of vitamin treatment were negative, this cannot be claimed as evidence that the children under observation had been receiving a sufficiency of vitamins A and D, nor as evidence that a deficiency of these vitamins, should it exist, is without influence on the course of measles. However, so far as the evidence goes, no benefit is to be expected from giving vitamin A or D to children admitted in the ordinary way to the

fever hospitals, i.e., usually after the appearance of the rash (which is generally reckoned as appearing on the fourth day of the disease) and for an average period of about three weeks.

Summary.

The effect of giving vitamin D, and vitamin D plus A, to children with measles was investigated on 697 cases under thirteen years of age at the North Eastern Hospital, London. The 697 cases were divided into three groups. The first group served as controls and had the ordinary ward diet only, the second group received in addition 3,000 international units of vitamin D daily as an emulsion of calciferol, and the third received the same amount of vitamin D, with, in addition, vitamin A equivalent to six drachms of cod-liver oil of a blue value of 7.5.

Comparison shows that on admission the children were fairly evenly divided between the three groups as regards age, incidence of pneumonia, and incidence of otorrhoea. They were also evenly distributed as regards the wards in which they were treated and the medical officers under whose charge they came. It so chanced that the D plus A group was at a slight disadvantage as regards sex and seasonal distribution and the stage of the disease at which the children were admitted, and the D group was slightly more favourably placed as regards sex distribution and the stage of admission. These differences were, however, slight. A comparison of fatality rates, of incidence of pneumonia, of otorrhoea, of all complications and of skin lesions developed in hospital, as well as a comparison of duration of pyrexia or of length of stay in hospital, affords no evidence of any favourable effect exerted on the course of the disease by giving either vitamin D or vitamins D plus A combined. It is pointed out that this negative result may be due (a) to the fact that the time of observation (average under twenty days) may have been too short to demonstrate any effect from vitamin therapy, and (b) that the treatment may have been started too late since in 81 per cent. of the cases treatment was not started until after the appearance of the rash, say till the fourth day or later in the disease.

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READING DIFFICULTIES IN CHILDREN

BY

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With an unimpaired sensory equipment and normal intelligence, every child learns to speak, and subsequently to read, write and spell his own language, so that his thought comes habitually to be verbally expressed. A study¹ of what was thought to be a case of congenital auditory imperception, but subsequently found to be a case of partial deafness, demonstrated the extent to which the various faculties required in achieving language are inter-related. In this patient, what was admittedly a severe degree of deafness but by no means a total deafness, led to a complete inability to acquire spoken language, the power to read, and to spell. Most of the individual letters were learned and remembered, but there was no facility at all for combining these into writing. A striking point in this case (an intelligent, partially-deaf, eight-year-old girl) was that her ability to hear and discriminate between different kinds of noises was excellent, but her deafness, affecting mainly the tone range covered by human speech, caused her own speech to be impaired and made her rely on sight and lip-reading for understanding. What bears on the present problem is the way in which the hearing loss had prevented her from learning to read, write or spell. For instance, the colour 'blue,' which she recognized, was named 'blulo,' but spelled 'lube,' and on another occasion 'bube.' In such ways her productions resembled those of children who, with apparently complete sensory equipment, have the utmost difficulty in learning to read. Ewing², describing his group of children with high frequency deafness, noted their failure in language development, and similar examples are given in the literature relating to congenital auditory imperception (Worster Drought and Allen³, Barton Hall⁴, and others).

A recent paper by Schonell⁵, from Goldsmith's College illustrates another side of this question of the inter-relation of functions in the faculty of speech. This deals with 'the relation between defective speech and disability in spelling.' Articulatory speech defects occurred in a large percentage (11 per cent.) in his group which consisted of 105 cases of specific spelling disability representative of a school population of 7,000 children. For instance, one child wrote:—

'The voxhe scerswie gro sue and wie gro viin, and we gro ruin and we gro groin. Sue fo no gin the sci, the due 5. Wie go in the vor and we cin we oio and uci wie go ba rine cothe, and co ba. Cuco wie sdand in the all and one of the sithe cu the civo no the dovo, the du the is of theco.'

TRANSCRIPTION.

'The Forster School we do sums and we do writing and we do drawing. Some of us get the stick, about 5. We go in the hall, we

sing, we pray, and next we go back in the classroom and go back. Sometimes we stand in the hall, and one of the teachers tells the story out of the Bible—the story of the Israelites.’

This example was from what Schonell called an instance of ‘intense paraphemia’ in which there was a lowered power of auditory discrimination in the realm of speech, although the cases studied could hear and understand spoken words. He speaks of the concomitant effect of backwardness in reading, but gives no figures indicating the extent to which reading was also affected. The point of common interest lies in this further corroboration of the close linkage between spoken language, hearing capacity, and the ability to learn to read, to write and to spell.

In spite of the extensive literature (see Jastak’s paper⁶) now accumulating on this problem, there is still some confusion of thought and much difference of opinion as to the fundamental nature of the disability. The lay mind, and most important, perhaps, the teacher, tends to assume that children who do not learn to read are obstinate, or stupid, probably both. This adds to the child’s difficulties, in that an attitude of scolding and disapproval comes to be associated with his reading lessons, and to some extent with all school activities. The figures given in this study, and those of other observers, confirm the impression, however, that the difficulty is certainly not confined to children with a general lack of intellectual ability. Nor does it appear to be the result of an inhibition primarily determined by emotional factors. Such an inhibition is certainly not the only cause, and probably not a common cause in the earliest stages of the condition. Later, no doubt, the ordinary child develops an attitude of resistance towards a subject which he finds difficult, although other children of his own age can learn it without any particular effort.

Mechanics and teaching of reading.

Before describing the investigations made on a group of cases seen at the Maudsley Hospital, a brief description of the mechanics and methods of teaching reading is given, together with some of the theories held to account for difficulties in learning to read. The idea of the investigation itself developed out of a study of these theories. The elementary school child usually receives some very simple instruction in reading and letters when he first reaches school and in a nursery school he may learn something of the kind before he is five. In English elementary schools, serious reading lessons begin as a rule when the child is about six. In preparatory schools of the modern kind, children may learn to read at five and teaching methods vary a good deal. The alphabet is no longer taught; letters are learned in association with pictures of common objects, and in the more modern type of school, the ‘look and say’ or sentence method is generally used. This encourages the child to recognize words, or larger units, as a whole, and to proceed from this to analysis of letter combinations, and their respective sound values. The fact that school is only begun at six years in the United States and that these methods are almost everywhere taught is thought to be the cause of the greater frequency of reading difficulties there as compared

with this country. In Germany the condition is much less frequent than here, perhaps because almost everywhere a phonetic method is used from the start, i.e., linking sounds to letters, and because of the more rational phonetic spelling.

The psychology of reading has been investigated, a good summary of this work being Vernon's book⁷, which has a full bibliography. She is mainly concerned with the mechanics which go to make a successful, facile reader. Certain points stand out, and have some bearing on the many theories which are held to account for the cases of difficulty.

The eye movements have been studied, and it appears that in all purposive looking the eye moves in a series of jerks directed towards focussing the object on the macula; during movement vision is not registered, so that to introspection, the eye appears to reach its object in a single sweep. In reading the jerks occur in a horizontal fashion with small backward lags, or even small movements in a reverse direction. Such wandering and wasteful movements are much more frequent in children who are just beginning to read, and resemble the irregular vocal 'reading aloud' of the bad reader. They are also more noticeable in reading material which is difficult of comprehension, and more so still when reading senseless jargon, or a foreign language, emphasizing the extent to which the mind, from familiarity with the written word, forestalls hesitation by guesswork.

Huey⁸ worked on an analysis of the important features determining the recognition of a word, such as the alternation of vertical letters and curved letters, using a tachistoscopical method, and there seems little doubt that, whatever the method taught, the end result in all normal readers is to recognize 'word-wholes,' rather than individual letters, proceeding to analysis by associated visual images.

Previous theories.

This leads on to the position taken up by the Gestalt psychologists, discussed in a recent paper by Frank⁹ on children with reading disability. She investigated three groups of children from London elementary schools: infants beginning to learn reading, children with pronounced reading disability, and a control group of normal readers. In the group of young children she found a tendency to confuse letters of great similarity such as u-v, m-n, b-d, and a tendency to remember the general configuration of a letter or word rather than its direction and orientation in space. In matching picture patterns, the most frequent mistake was to confuse one pattern with its mirror image. Such children were also unable to synthesize different sounds and letters into a word, and similarly had difficulty in separately recognizing the individual letters in a word. In giving her conclusions she draws attention to the well-known faculty some children possess of recognizing apparently identical objects such as different gramophone records, or the notation of a song without being able to read music. Her conclusions are that it is typical of the infantile perception to see wholes, to recognize shape and solidarity of an object, rather than to perceive detailed differences in the direction, for instance, of component parts. She found that the poor readers tended to reproduce very similar errors, and she suggests that the backward reader is one who remains 'on a relatively immature level of perception' and therefore implies that this fusion of wholes is a method of perception which the normal child outgrows. Her remedial work aimed at teaching and encouraging the child to improve its recognition of whole words and sentences. It is interesting that this

view is almost diametrically opposed to that of a group of American psychologists, and to Hinshelwood, who advocates the phonic method in re-educating these children.

Since Hinshelwood¹⁰ first drew attention to these cases (although many isolated examples had been published prior to this), there has been a desire to postulate an organic basis to account for the findings. His book begins with a description of a case of acquired word-blindness with right homonymous hemianopsia. He notes the failure to recognize words, to remember and name the individual letters, to link letter-sounds into words, that is to write and to spell, and the ready fatigue and variable attention which accompanied efforts to do so. The lost associations were extremely difficult to re-form, but the localization of the lesion limited its effects to letters as symbols, the memory for figures and recognition of them remaining intact. He then describes a group of children in whom a somewhat similar condition, without hemianopsia, existed. In one, the familial occurrence was striking and to him suggested a developmental anomaly. He implies that such an anomaly must exist and differentiates between the severe case for which the term congenital word blindness should be reserved, and suggests congenital dyslexia for children who merely find it difficult to learn to read. He makes no analysis of the types of mistakes most commonly made, and does not suggest that there may be gradation, rather than a difference in kind, between the severe and the mild case.

Orton's¹¹ theory involves the conception of different levels of cerebral function, postulating that the ability to perceive visual stimuli and to register that perception, is located in cells around the calcarine fissure of the occipital lobes, and that localization is arranged, by means of the decussation of the optic tracts, in such a way that the right visual field in both eyes is represented at the right occipital pole, and the left field at the left pole. At a higher level, in the physiological sense, and probably located immediately peripheral to the calcarine fissure is a visual-recognitive area, bilateral destruction of which causes visual agnosia, that is, the non-recognition of perceived objects, while the third level, the visual-associative, gives the recognition and understanding of written symbols, that is to say, of words, the area concerned being the left angular gyrus when the left is the dominant hemisphere. He suggests that visual memory patterns, or engrams, are formed in both hemispheres, those in the dominant hemisphere being the ordinary right-handed form of the written word, and those in the so-called silent hemisphere being the mirror image, thus CAT and TAC, and that the brain learns to suppress the mirror image. He similarly supposes that the pattern of kinaesthetic memory images may be disturbed so that a tendency to move from the centre of the body outwards, as in writing with the right hand, and reading from left to right, may be altered to a sinistral direction, as in mirror writing with the left hand.

With this theory he attempts to explain the frequency of what he calls 'static' reversals of letters, for instance 'b' being confused with 'd,' 'p' being confused with 'q,' and 'kinetic' reversals of words or parts of words, such as 'saw' being read as 'was,' and 'ton' being written or read as 'not.' Children with a reading difficulty often misread such a word as 'tarnish,' saying 'tarshin,' and they show a greater facility than the normal child for mirror reading.

Here, therefore, is a relation to the question of dominance. One of the few facts that is generally accepted in this question of speech localization, is that in right-handed people the hemisphere controlling the more highly perfected motor movements, is also the hemisphere in which the speech centre is located. Tests have been devised to establish ocular dominance. There is a good deal of evidence that man has a leading or preferential eye,

as definitely chosen from the other as is the leading hand. Obviously eye dominance of which the subject is unaware, is less likely to be interfered with by education, and so may be a fairer test of lateral dominance as a whole. Some interest attaches therefore to the relatively high proportion of left-eyed children who have reading difficulties. On testing the handedness, and 'eyedness' of normal children, and those with difficulties in reading, there is a greater proportion of mixed dominance. To explain this more fully, the normal person is right-handed, and right-eyed. But a few people are left-handed and left-eyed. But some normal people, and a rather larger proportion than normal of cases of reading difficulty, are right-handed and left-eyed, or left-handed and right-eyed. It is certainly an observed fact that the group of children with reading difficulties tend to show this mixed dominance in higher proportion, and are often unduly late in establishing manual dominance, or there may be a history of left-handedness in near relatives.

According to Orton this is due to a developmental delay in assigning dominance to one hemisphere, and consequently to a longer persistence of the tendency to reverse directions in reading and writing, and so to the persistence of a difficulty in eliding the reversed image and consequent confusion and difficulty in reading. In Monroe's¹² cases, and in the material described in this paper it will be seen that the children with reading difficulty did show a relatively high proportion of mixed dominance. It is by no means clear, however, that this fact by itself would be regarded as evidence of the validity of Orton's interesting but speculative theory. As has been shown, Frank would interpret it otherwise. Dearborn¹³ has compared and recorded the eye movements in normal readers, and children with reading disability, and has emphasized other ocular factors, such as muscular imbalance, and Selzer¹⁴ has added to the theories by his work on suspensopia, or alternating vision, a point which he relates to lateral dominance. A recent article by Eames¹⁵ attempts an anatomical corroboration by assuming that longer association paths must exist, with greater liability to interference, when hand and eye preferences are situated in and controlled from different hemispheres.

In attempting to assess the value of these theories, the absence of exact knowledge is more striking than their validity. Each investigator describes a number of cases and brings forward evidence, so that each theory is up to a point supported by well-documented clinical findings. Of these, the anatomical may be expected to be hard to find, since these children live and outgrow their condition, and it appears as unreasonable to look for measurable developmental failure here, as in, say, a case of outstanding lack of musical appreciation. The impression which gradually evolved during the present investigation is that all the theories have some bearing, and that none is wholly satisfactory because the cases do not fall into a single category. This only serves to emphasize again the complex factors involved in the acquisition of a written language. Thus, the recognition of arbitrary but accepted symbols, the formation of linkages between these and auditory images and memories, the kinaesthetic factors, notably in writing, and the intelligence and interest which the child brings to bear on the problem, must all play a part.

Present investigation.

This particular study was undertaken with a view to seeing how far these cases of reading disability could be compared with other forms of aphasia, both congenital and acquired, particularly with reference to the views and theories put forward in the literature. It was carried through with the help and co-operation of Dr. W. Mayer-Gross, to whom I am indebted for many suggestions, both in actual procedure, and in analyzing the results.

The material (fifty cases) was obtained from the Children's Out-patient Department at the Maudsley Hospital. The method of selection was to take those children who were referred for difficulty in school work, or in whom, after initial interviews with the psychiatrist and psychologist, such difficulties appeared to be present. It is the usual procedure, in all cases referred to this clinic, for the psychologist to give an intelligence test, comprising the Burt revision of the Binet-Simon scale, some performance tests, and a selection of Burt's educational tests, and the children in this series either complained of a difficulty in reading, or were found by testing to have a reading age two or more years retarded below their mental age. Thus a simple range of tests can give a summarized picture of a child's abilities and attainments. Typical examples, given below, can be transcribed into graphic form, to which Munroe gave the name of 'educational profile' (table 1).

TABLE 1.
TYPICAL EDUCATIONAL PROFILES.

CASE AND SEX	CHRONOLOGICAL AGE	MENTAL AGE	I.Q.	READING AGE	ARITHMETIC AGE	
1 K.C. M.	9 $\frac{9}{12}$	9 $\frac{10}{12}$	102	5 $\frac{9}{12}$	10	Typical reading disability
2 D.H. F.	8 $\frac{9}{12}$	8 $\frac{8}{12}$	98	6 $\frac{7}{12}$	7 $\frac{4}{12}$	Less severe case with some general learning disability
3 E. McC. M.	11	8 $\frac{6}{12}$	77	6 $\frac{6}{12}$	9	General backwardness, but arithmetic well up to (actually above) mental age though still below chronological age
4 D.R. F.	10 $\frac{7}{12}$	8 $\frac{7}{12}$	80	8 $\frac{6}{12}$	8 $\frac{6}{12}$	General backwardness; both reading and arithmetic barely up to mental age

Special tests.—The following scheme of special tests was evolved by Dr. Mayer-Gross, with the idea of estimating the various capacities utilized by the child in learning to read, but arranged, so far as possible, without the use of letters. They were usually described by the children as 'puzzles.'

A series of cards was made in duplicate bearing arbitrary patterns, using straight lines, dots or geometric figures. One set was placed on the table, and the child was asked to match each one with the duplicate set of identical cards handed out to him. This test was within the intellectual capacity of both the youngest and the dullest child seen, and it at once became obvious that in ordinary ability to recognize a simple visual pattern, these children were not significantly below the average. More mistakes were made by mentally dull children than by those who, in reading, frequently would confuse what seemed to us relatively simpler shapes, such as b and d.

They were then asked to copy a pattern made from coloured mosaics, and then reproduce the pattern from memory. Here a few children tended to get the general configuration of the pattern correct, but would make a mistake in direction, although this never extended to making a true 'mirror image' pattern. Out of the fifty children tested, only five tended to alter the direction only, and of these five one was a borderline case with an I.Q. of 70.

The children were then asked to listen to a simple rhythm, tapped on the desk, and to reproduce this rhythm; in many cases, the memory for such a simple auditory pattern was excellent, but in some, often the restless and hyperactive children, the pattern would soon be lost. One particularly interesting group, discussed below, was singled out by this test.

To estimate how far kinaesthetic factors were involved, and whether the children could recognize by touch, the shape of letters and figures, a series of wooden capital letters was used. After making sure that these could be named by sight, the child was blindfolded and given a letter in the hand. Also after getting the child to write down the numerals, again to make sure that these were known, a selection of numbers was traced on the dorsum of the hand with a blunt pencil, and the child's arm passively moved in the air to form a numeral, both tests being done with the child blindfolded. He was then asked to 'guess' what had been 'written.'

Only six children showed any marked tendency to reverse the numbers in writing them to dictation. This is in contrast to the persistent tendency to reverse letters such as b and d. Some of the younger children failed to understand the directions, and in the group as a whole, the results were not sufficiently consistent to give any very significant information. What again became clear was that many children, who failed to recognize written letters visually, and who made mistakes both in writing and reading them, had no such difficulty with figures.

It must be understood that these tests were not applied with the idea that statistical results would be forthcoming. They are not standardized tests, but they served the purpose of illustrating the extent to which ancillary factors in the acquisition of reading remain intact in children who yet fail to learn to read.

In the older children, and those who could make some attempt at reading, the tests described by Monroe¹⁶ as Iota word test, and Word discrimination test were used. These are useful for drawing attention to the tendency these children have to confuse 'mirror-image' letters such as b and d, p and q, to reverse directions reading 'not' for 'ton' and the present results tallied with hers, although the small numbers debarred any attempt at statistical analysis. Each child was also tested for handedness, and eyedness, both by the psychologist, and on another day, by the author. The validity of the eyedness tests was not certain, but using the same tests, on separate occasions, the results of both investigators tallied perfectly.

Results.

The sex distribution shows a preponderance of boys over girls, this being a usual finding in all investigations relating to speech and language

ability. Orton¹⁶ brings this into his work on stammering, suggesting that the greater prevalence of this in males is an effect in the motor and kinaesthetic component of speech in the same way that severe reading disability is a failure in the visual component. It is interesting to note that stammering is known to follow attempts to make a naturally left-handed child use his right hand, perhaps by dispossessing the newly-acquired habitation of the speech centres. In the present series of fifty cases, there were thirty-eight boys with ages ranging from 6.3 years to 14.8 years, and twelve girls with ages ranging from 7.6 years to 13.1 years. In Monroe's series, the preponderance of boys (84 per cent.) over girls (16 per cent.) is even higher. Handedness, and eyedness tests gave the results shown in table 2. These figures can usefully be compared with a similar group of

TABLE 2.

HANDEDNESS AND EYEDNESS.

	MAUDSLEY CASES		M. MONROE CASES		CONTROLS	
	PER CENT. OF TOTAL		PER CENT. OF TOTAL		PER CENT. OF TOTAL	
R. H. AND R. E.	24*		47*		59*	
R. H. AND L. E.	18	†	35	†	21	†
L. H. AND R. E.	12		3		6	
L. H. AND L. E.	12		8		5	
R. H. AND AMBI E.	6		6		9	
L. H. AND AMBI E.	2		1		0	
AMBI H. AND R. E.	16		—		—	
AMBI H. AND L. E.	8		—		—	
AMBI H. AND AMBI E. ...	2		—		—	

Compare * with † in pathological and normal cases.

cases, and controls cited by Monroe in her book. The point to note is the relatively high percentage of mixed dominance, that is L.H. and R.E. or R.H. and L.E., compared with those children who were fully right or left dominant.

In the fifty cases studied, the range of intelligence quotients showed wide variations (table 3).

TABLE 3.

INTELLIGENCE QUOTIENTS.

I. Q.	NO. OF CASES.	}	
70 - 80	13 CASES		
80 - 90	20 CASES		DULL AND BACKWARD GROUP.
90 - 110	16 CASES		NORMAL GROUP.
OVER 110	1 CASE		

In a smaller group of twenty-one cases, selected for more intensive study, six cases have an I.Q. of over 100, the highest being 107 (two cases),

thirteen cases have I.Q.'s between 83 and 98, and only two have I.Q.'s of 73, these two being included because of special points in the family history. This is a usual distribution for London elementary school children, and suggests that there is no dearth of material among the ordinary school population.

The rhythm test separated out a small group of interesting cases. It was found that out of the fifty children, nine, who showed no difficulty in any other test, failed completely in this one. Table 4 shows that these

TABLE 4.

RHYTHM TEST SUB-GROUP.

NAME	AGE	I.Q.	AGE ON TALKING	MOTOR AND SPEECH ABNORMALITIES
JOHN S.	11 $\frac{4}{12}$	102	'NEARLY 3'	Slight stammer and speech defect.
EDWIN S.	8 $\frac{11}{12}$	95	2 $\frac{1}{2}$ -3	Restless and fidgety.
DENYS S.	9 $\frac{2}{12}$	89	2	Aggressive—has had slight chorea.
HARRY L.	11 $\frac{11}{12}$	107	NORMAL	Left-handed and clumsy.
BRIAN H.	6 $\frac{9}{12}$	103	3	Stammers, twitch (tic) of face.
HENRY H.	6 $\frac{3}{12}$	93	3	Fidgety and aggressive.
ARTHUR H.	13 $\frac{3}{12}$	86-90	2	Speech defect and slight deafness.
JOHN D.	10 $\frac{8}{12}$	112	2+	Motor control very poor.
SIDNEY O.	10 $\frac{1}{12}$	94	2+	Motor control poor; has squirming movements.

were all children of good intelligence, with noticeable hyperkinesis, and with one exception outstandingly late in learning to talk. The association of a failure in auditory memory with retarded speech suggests an auditory factor. Whether or not the hyperkinetic tendencies are more marked in this group than in others is not yet clear. A number of these children are certainly hyperkinetic, with poorly executed movements and often the description of 'fidgety, restless, and inattentive' is given by the school. The degree of hyperkinesis was sufficient to be noted as increased in the summaries of twenty-two of the present fifty cases. This is naturally difficult to standardize or estimate quantitatively, and the apparent clumsiness often interferes very little with actual achievement of something the child likes doing, such as performance tests, jig-saw puzzles, or building bricks. Sometimes, however, this restless inattention has been noticeable during testing, and being such an outstanding trait might well have led to yet another theory as to the causation of reading disabilities.

All the children show mistakes which make Orton's theory a tempting one; and no other 'school' has attempted to explain the extraordinary frequency of certain confusions and the way in which all types seem to repeat certain standard errors. It would seem as if, bearing in mind only similarity, such words as 'sun' and 'sum' 'tool' and 'fool' might be confused. And yet such a mistake was never noted, although 'saw' and 'was' were often confused. In Monroe's analysis of errors, while the

children with a reading disability, and normal children learning to read, produced the same errors in many cases, the reversals, confusion of mirror-image letters, and palindrome words were in excess, and tended to persist, and to be repeated in subsequent tests, in the children who had a marked degree of reading disability.

Auditory factors are certainly present in some cases, and without an audiometer it is extremely difficult to make any accurate hearing test in young children. It seems certain, however, that difficulties in auditory discrimination and reproduction may occur even with apparently perfect hearing, and Schonell's work indicates the extent to which imperfect speech and auditory imagery for words may affect spelling. In two of the present cases it has been possible to get an audiometer test done.

Both boys had what was regarded loosely as 'normal hearing.' Both made mistakes in words, for instance A. H. heard 'southern' as 'sudden,' and 'Mars' as 'mask,' and is slipshod in his own enunciation of words. The other boy, L. O., pronounced poorly, and he misheard several words in a vocabulary test; he could not analyze words into their constituent sounds. In this case, reversals and confusion of seen letters were not at all marked, for instance he had no difficulty in distinguishing b, d and p, q. An audiogram of both these boys shows a small loss in auditory acuity affecting the area of tones used in human speech.

Certainly all these children have great difficulty in blending sounds into words, and in analyzing a difficult word into its constituent sounds. A common reply is 'I don't know that one' to a rather more difficult word, the child not yet having grasped that reading as a process is universally applicable, once the linkage between sound and letter has been accomplished.

Finally, the question of the importance of the family history was considered.

Hinshelwood, describing his famous group of cases, had under observation a family including four brothers, none of whom succeeded in learning to read while at school. The children, a boy and a girl, of an elder sister of these boys, also experienced the greatest difficulty with reading. In all six cases, the difficulty was specific for reading, and in other ways the children seemed bright and intelligent.

In the present series, the family history was studied from two aspects, namely, the question of left-handedness, with or without stammering, and the presence of severe difficulty in reading in either parent, their siblings and offspring or grandparents. The significance of this is impossible to assess with any accuracy, since remarks were often of a general kind, such as 'he was always slow in school.' In few cases could the relative, of whom this was said, be interviewed, and it was often forgotten whether the 'slowness' referred particularly to reading. Accepting this low standard of accuracy, there was a positive family history in seventeen of the fifty cases. In six cases, there was left-handedness in one or more near relative (as above), and in three further cases, this left-handedness went with an observed difficulty in learning to read, and in eight cases there had been some members of the family with difficulty in learning to read or in school work generally.

Emotional aspects.

Something remains to be said concerning the emotional aspects of the problem. While not wishing to claim for this condition of reading disability the degree of specificity with which some authors have endowed it, yet it seems clear that these cases are too much alike, too clear-cut, the familial tendency too marked, to allow of an explanation on a neurotic basis alone. Hollingworth¹⁷, and in a recent paper Blanchard¹⁸, have rightly pointed out the extent to which children who are emotionally disturbed may become unable to progress in school work. In this clinic some children have been seen, with almost complete inhibition of all the normal learning processes.

Such a boy was R. G., aged 9. His mental age was 8, reading age, 7½, and arithmetic age, 6-7 years. He was a moody, over-quiet, preoccupied child, obviously worried and compensating for this by living in a world of fantasy. His arithmetic was as severely retarded as his reading. When he could be persuaded to emerge from his fantasy life, his performance, though requiring an abnormal amount of encouragement and stimulation, gave results not far below that of a normal child of his age, although in school, at nine years old, he could barely keep up with seven year old children. He showed none of the restless inattention, or aggressive over-compensation which came to be associated with the children tested and found to have a specific reading disability.

At this stage in the investigation cases could certainly be distinguished in which emotional tension had become expressed as a symptom, in one child, in reading difficulties, in another child as motor disturbances such as ties, and in another as, say, a regression to nocturnal enuresis. Further, the secondary neurosis, which certainly does occur, and may be due to many factors, must be taken into account. By the time the case reaches the clinic, the child has usually been accepted as 'silly' by fellow pupils and backward by his teachers. His grotesque compositions, such as that given below in the case of A. H., are held up to the class for ridicule. What is perhaps worse is when he is regarded as obstinate, and constantly receives such reports as 'could do better if he tried,' and 'lacks concentration.' The fact is, that, like all true aphasics, his memory for words and letters is erratic, and his associations, made one day, are forgotten the next, while his attention is extremely readily fatigued. In this connection, one feels that Head's description of his re-education of aphasics might be circulated in schools. Such difficulties may carry over into the home situation, where he is outstripped by younger siblings. Parents may either be sceptical of his efforts, or over-anxious and inclined to blame the school, or, having had a similar difficulty themselves may show concern at having handed on such a tendency, or may advocate that the child be left to 'grow out of it' as they have probably done. These children therefore tend to dislike all school, and so to truant, or to play the fool while there, or they may attempt to over-compensate by an interest limited to handwork or games. They cease to have any interest in books, and behaviour problems may develop in association with unoccupied leisure within or outside school hours.

In so far as these children have any sort of emotional difficulty common to the group, it would seem to be an aversion to effort showing itself in distractibility, restlessness and lack of interest in books, and granted some common basis for the initial difficulty in reading, it is easy to see how the habitual evasion of that difficulty will tend to set up faulty associations, and a persistence of these, until the mistakes become a habitual reaction. Not the least interesting part of the remedial teaching and re-education of these children is the effort which must be made to begin the new 'reading' work on lines and material far removed from that to which the child has become so drearily and pessimistically accustomed.

Detailed case records.

The three case studies show examples of differing types. In A. H. the personality problem is uppermost, and after careful observation it is concluded that it seems to be primary rather than secondarily determined by his school failure. In J. D. the hyperkinesis was so marked that his writing showed a decided tremor. There is over-compensation in the form of boasting jocularity. J. R. has a stable temperament and illustrates the effects of familial incidence. His progress with coaching is less rapid than would be expected with such an intelligent and willing pupil.

Arthur H., aged 13 $\frac{1}{2}$, had a mental age on performance tests of 11 $\frac{5}{8}$ or higher. His reading age was 6 $\frac{1}{2}$, and spelling age 7 $\frac{1}{2}$. At his age the Binet scale is inapplicable because of reading being a necessity. He was a peculiar shy introverted boy, persistently truanting from school, often bullied or teased by other boys, fond only of woodwork, and of going to the cinema. In hospital he tended to evade any difficulty, but was co-operative provided he was encouraged and stimulated. Otherwise he would 'slack' and be slovenly in his appearance. His power of verbal expression was poor and he made mistakes. For instance, telling a story he said, 'once upon a boy, there was a boy,' and 'he killed the gold head that lays the gold eggs,' noticing no error. He copied correctly, but his written composition was almost unintelligible. He was told the 'Cowboy Story'—

A cowboy went to San Francisco with his dog, which he left at a friend's house while he went to buy a new suit of clothes. Dressed up in his grand new suit he came back to the dog, whistled to it, called it by its name and patted it. But the dog would have nothing to do with him, and did not know him until he changed back into the old suit of clothes.

His version ran as follows:—

He went to with his bog which he laft as a fuleds whil he went to buy a mew soit of coset Destir in his grand mew soit he came back to the dog whicld to it called it bay it name and part it bag the dog wood not have nufist to d with him in new hat and coat.

Another composition of his ran:—

Dear Mother I has a very happy Xams. There has been a pary in hour ward we had rot factd for dinner.

(Dear Mother, I had a very happy Christmas. There has been a party in our ward, we had roast turkey for dinner.)

His progress with coaching was completely erratic and words learned one day would be completely forgotten the next. He realized his difficulties, often reading longer words such as 'gramophone' more easily than a word like 'thought.' His evasive, aloof attitude rendered special teaching a laborious and all but futile procedure.

John D., aged $10\frac{1}{2}$, had a mental age of $11\frac{1}{2}$, I.Q. of 107 and reading age of $7\frac{1}{2}$. A boastful hyperkinetic boy, with great difficulty in reading, he could spell orally but his written spelling was atrocious. He was concerned about his school failure. At the clinic he 'showed off,' had many comic mannerisms, and only under pressure produced writing or spelling or would agree to read. He guessed wildly, and once broke off to say 'my brother got a prize for this.' He was explicit about this jealousy towards the younger sibling: 'I noticed the difference when he came but I've got over minding.' He showed jerky, poorly controlled movements; his associated movements were much increased, writing was shaky, but drawing and handwork were generally very good. He improved slowly and steadily with coaching, but for a long time failed in grasping configuration of letters, and mechanics of reading. Now aged $11\frac{1}{2}$ he is up to standard in school, except in spelling, which is still erratic.

Jack R., aged $8\frac{1}{2}$, had a mental age of $7\frac{1}{2}$, I.Q. of 97, and reading age of 4.8. He was quiet, stolid boy, big for his age, happy and popular in school. He was good at oral work, backward in reading and all written work. His mother was intelligent, but herself could not read until aged twelve. Her sister was late in reading and a brother, now a master carpenter working from blue prints, could not read till sixteen, hence secondary anxiety in the mother at having handed on her peculiar difficulty. The boy was for long ambidextrous, but is now right-handed and right-eyed. He frequently confused b-d, p-q, and occasionally reversed figures. He mistook vowels reading 'melk' for 'milk,' 'sun' for 'sin,' and read 'crad' for 'card.' He showed an excellent attitude, interested and plodding, to coaching, but progressed only slowly at first. He is now only sixteenth in class of thirty-six.

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THE USE OF AVERTIN FOR THE PRODUCTION OF BASAL NARCOSIS IN CHILDREN

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The introduction of avertin has been described as the most important discovery in anaesthesia for many years¹, and one of the greatest of the benefits which it confers is the complete amnesia provided by this substance for children about to be submitted to the otherwise terrifying ordeal of inhalation anaesthesia. All observers are agreed that the psychological trauma inflicted on the patient by the ordeal of an operation is naturally greater in the case of children than in the majority of adults. The attendant circumstances of the induction of inhalation anaesthesia are obviously the cause, this being the only part of the proceedings of which the patient is conscious. This psychological trauma may be hidden, but it is soon apparent when—sometimes many years later—a child becomes aware that it is again to be subjected to the induction of inhalation anaesthesia. An anaesthetist witnesses few scenes more disturbing to all concerned than the abject terror so often displayed by the unfortunate child in these circumstances. Before the introduction of basal narcosis, the child was frequently submitted to the ordeal of being suddenly taken from his accustomed ward and confronted with the strange surroundings and strange faces in the ante-room of the theatre, followed by varying degrees of apprehension until he received the crowning horror of feeling suffocated by the anaesthetic mask placed over his face. The introduction of basal narcosis by means of methods both reliable and safe has made it possible entirely to abolish this undesirable accompaniment of operation. It is, in fact, hardly an overstatement to say that, excepting in case of urgency, or other exceptional circumstances, no conscious child should ever see the theatre or be submitted to the terrors associated with the induction of inhalation anaesthesia.

Although the psychological aspect is, in the case of children, obviously pre-eminent, it is by no means the only benefit conferred by the use of basal narcosis. Other advantages are:—

(1) Subsequent full surgical anaesthesia can often be maintained by the use of gas and oxygen alone, or, if necessary, with a greatly reduced amount of ethyl chloride or ether.

(2) The post-operative period is one of much greater comfort and well-being for the patient. Amnesia often persists for several hours after operation, although the patient will often take drinks and talk apparently quite rationally during this period.

(3) The reduced amount of ether used tends to diminish the occurrence of post-operative vomiting and of respiratory complications of anaesthesia.

Choice of drug.

Many drugs are commonly used to produce basal narcosis, chiefly avertin, paraldehyde, or one of the barbiturates (nembutal, evipan or pernocton). Of these, avertin stands pre-eminent, particularly for children. The comparative advantages of avertin may be summarized as follows:—

(1) Avertin in ordinary accepted dosage (0.075–0.1 gm. per kgm. body-weight) is particularly safe for children, because they tolerate the drug extremely well. Avertin constantly produces a greater depth of narcosis in adults than in children. This tolerance has recently been confirmed by Boyd² who claims to give avertin safely in massive doses (up to 0.2 gm. per kgm.) to children in order to produce full surgical anaesthesia, a procedure unanimously condemned by leading authorities in this country^{3, 4}.

(2) Unlike many of the barbiturates (unless the latter are administered by the intravenous route, which is usually difficult in children under the age of five years) avertin always produces complete amnesia. The action of avertin is certain, and largely uniform, whereas that of the barbiturates, e.g., nembutal by mouth or by rectum, is uncertain and capricious.

(3) Restlessness during the induction of unconsciousness with avertin is uncommon. Loss of consciousness is unattended by any unpleasant subjective sensations, and the patient presents the appearance of natural sleep, rarely moving from the position adopted for the administration of the avertin.

(4) Post-operative restlessness after avertin is less common, particularly in the case of children, than after the use of a barbiturate.

(5) Avertin has little appreciable effect on the chief organs of excretion, i.e., the liver and kidneys. Too much unwarranted prejudice still exists against avertin on this score, but with the increasing experience that has been gained since the introduction of the drug to England in 1929, the greater is the tendency of authoritative opinion, based upon both clinical^{5, 6}, and experimental^{7, 8, 9} evidence, to regard the toxic effects on the excretory organs as negligible. It is, for instance, as yet insufficiently realized that avertin is less toxic than ether, and is completely non-irritating to the respiratory passages.

(6) Avertin, unlike paraldehyde, has no appreciable odour at a distance of more than a few inches from the flask containing the solution. Paraldehyde is still widely used as a basal narcotic for children, largely on account of the reputed safety of the drug. The writer's experience of paraldehyde is small, because it does not appear necessary to subject the attendants of the patient to the unpleasant, nauseating odour of this drug when avertin provides an equally safe or safer alternative. Moreover, the action of paraldehyde is less uniform than that of avertin, and many cases have been reported in which alarming signs of undue respiratory depression have developed in the post-operative period^{10, 11}.

(7) Avertin is rapidly absorbed from the lower bowel¹², which relieves the attendants from the necessity of washing-out any remaining solution after the patient has returned to bed.

There is no doubt that the use of avertin has largely superseded that of paraldehyde for adults, and the next few years will probably show the same trend in the case of children,

Avertin has two disadvantages: (1) The correct preparation of the solution requires time and care¹³. (2) If the condition of the patient, following a severe operation, is such that rectal salines are indicated, these are not well retained during the first four or five post-operative hours. This disadvantage is common to all narcotics administered per rectum.

Contra-indications.

There are three definite contra-indications to the use of avertin:— (1) Whenever it is impracticable either to obtain or accurately to estimate the weight of the patient; (2) the presence of pathological conditions of the rectum or colon; and (3) operations on the rectum or colon. Two relative contra-indications which are subjects of controversy among leading authorities are:—(1) The presence of 'moist' breath-sounds; and (2) impaired liver function. Sir Francis Shipway states that the presence of bronchitis is not a contra-indication for the use of avertin¹⁴. Although the writer has administered avertin without harm on three occasions to patients suffering from active bronchiectasis, his inclination is to deprecate the use of avertin under such conditions, as tending to delay the rapid return of the maximum respiratory efficiency so desirable in such cases. In spite of contrary expression of opinion¹⁵, the trend of clinical evidence seems increasingly to be that avertin may be used with safety even in the presence of grossly damaged liver function^{16, 17}.

Avertin plus nitrous oxide and oxygen have recently been successfully administered to a boy aged twelve years for the purpose of a resection of his splanchnic nerves in an effort to mitigate an uncontrollably severe diabetic state. On the morning of operation his blood-sugar content was 170 mgm. per 100 c.c. Operation was performed in the afternoon. In the evening his blood-sugar content was 150 mgm. per 100 c.c. During the following forty-eight hours, the blood-sugar content was as follows:—

1st morning	135	mgm.	per	100	c.c.
1st evening	145	"	"	"	"
2nd morning	140	"	"	"	"
2nd evening	70	"	"	"	"

This case provides a particularly striking example of the low toxicity of avertin.

The conclusion has been reached, based on personal experience of nearly 1,000 cases, that, except in the presence of the graver emergencies of surgery, if a patient will tolerate any anaesthetic at all, avertin may always be given with confidence and safety.

Technique of administration.

Although the following description applies particularly to the use of avertin for routine sessions for operations for the removal of tonsils and adenoids, it is equally applicable in individual cases for other operations. It is based on a series of 5,918 administrations at the Booth Hall Hospital, Manchester, where this method has been employed for the last six years.

Preparation of the patient.—The children are admitted the day before the operation. In non-abdominal cases, unless the parent reports that the child suffers from obstinate constipation, no aperient is necessary. A simple enema is administered about 6 p.m. The evening meal should include glucose, either in the form of jam or syrup, or, alternatively, each child may be given $\frac{1}{4}$ lb. of boiled sweets. Four hours before operation a simple rectal wash-out is administered. Three hours before operation each child receives a plate of porridge or gruel, together with a liberal helping of syrup.

Preparation and dosage of avertin solution.—The weight of each patient should be entered in writing on the temperature chart, and the name, weight and required dosage of avertin for each patient should be sent to the dispensary in writing. Telephonic or verbal transmission of these particulars should be prohibited in order to prevent mistakes. The usual dosage for cases in which operations are to be undertaken on the air passages, and in which a rapid return of the cough-reflex is consequently desirable, is 0.075 or 0.08 gm. per kgm. body weight. For operations other than those on the respiratory passages, a full dose of 0.1 gm. per kgm. should be prescribed. Avertin is administered as a 2.5 per cent. solution in distilled water. The description of the actual preparation of the avertin solution is outside the scope of this paper, and may be obtained elsewhere (Bayer Products, Ltd.), but the recommended method should be strictly adopted. For a long list of cases, in which each patient receives the same dosage of avertin (e.g. all 0.075 gm. per kgm. body weight) the simplest method of procedure is to prepare in bulk the total quantity of avertin solution required, and then to measure out from this the requisite amount for each child. The required solution can be prepared in fifteen minutes. The bottle containing the prepared solution for each patient should bear a label stating the name and weight of the patient, the quantity of avertin fluid and water used, and the date and hour of preparation. These particulars should be checked by the ward-nurse against those on the temperature chart before the actual administration is begun. These precautions may seem to be unnecessarily severe, but rigid adherence to these rules is the only adequate safeguard against the possibly disastrous results of administering the wrong dose to the wrong patient.

Administration.—Thirty minutes before the time of operation, the child is placed in the left lateral position, and the solution is run slowly into the rectum by means of a small catheter, tube and funnel. Administration should be slow, taking up to ten minutes to complete. Immediately afterwards, the child should receive a dose of atropine, graduated according to age as follows:—

AGE OF PATIENT.					DOSAGE.	
0-3 MONTHS	NIL	
3 MONTHS 1 YEAR	$\frac{1}{200}$	GRAIN.
1-2 YEARS	$\frac{1}{150}$	"
3-5 "	$\frac{1}{120}$	"
5-12 "	$\frac{1}{100}$	"
12 YEARS OR OVER	$\frac{1}{60}$	"

The child should then be left quiet, when it usually drops off to sleep within fifteen minutes, and often before the administration is completed. It is then transported to the ante-room of the operating theatre to await operation. At this stage, it can easily be roused by light stimulation, such as pinching the skin, and will invariably resist the application of a mask when the administration of ethyl chloride or ether is begun, but amnesia is always complete.

Surgical anaesthesia after premedication with avertin.

The administration of ethyl chloride or somnoform—preferably by means of a bag—suffices for the production of surgical anaesthesia for the removal of tonsils and adenoids by the 'rapid' technique. Induction of anaesthesia by this method is rapid, and the face-piece, or mask, should be removed as soon as the child has taken three stertorous inspirations. One of the great advantages of avertin is to increase the time available for the performance of the operation after the face-piece or mask has been removed. For other surgical operations, or for more leisurely removal of tonsils, including, if necessary, the insertion of a Boyle-Davies gag, anaesthesia should be induced by means of an ethyl chloride-ether sequence administered on an open mask, and anaesthesia subsequently maintained with ether, or, for procedures other than intra-abdominal or oral operations, with nitrous oxide and oxygen.

The only disadvantage of the use of avertin is that the amount of haemorrhage at the operation is slightly increased. This, however, is a temporary, and therefore unimportant phenomenon, as is proved by the fact that the incidence of reactionary haemorrhage is not increased.

Post-operative treatment.

The safety of this method of anaesthesia depends on scrupulous attention to the following points after the operation is concluded:—

(1) The child must not be removed from the operating theatre until the cough reflex has returned. If the 'rapid' technique has been used, this reflex usually returns within one minute of the conclusion of the operation.

(2) The child must not be left with the airway unattended during transport back to the ward.

(3) After return to the ward, the same precautions regarding the airway must be observed until all danger of obstruction is past.

The use of a 'recovery' room adjacent to the operating theatre is of enormous value in facilitating the post-operative care of all patients who have undergone anaesthesia. It may be thought that this procedure involves undue loss of time, and necessitates the presence of a large number of attendants, but with careful organisation such is not the case. It is not necessary to have one nurse for each child. By giving avertin to the first child fifty minutes before operation (the exact time of administration is not important provided that it is within the limits of fifty to thirty minutes before operation), three or four children may be transported on one trolley, in charge of one nurse, to await operation in the ante-room. After the operation, the same procedure may be adopted, and the children re-transported to the ward in batches of two or three. The use of avertin abolishes the necessity for segregating the children awaiting operation in a separate ante-room, and thus eases the task of the supervising nurses.

Complications following the use of avertin.

Although, with a single exception, no complications following the use of avertin have occurred in this series of cases, no description would be complete without a reference to the signs and treatment of an overdose. These are those common to all narcotic drugs which, in large doses, cause a progressive paralysis of the medullary centres—profound unconsciousness, slow and shallow respirations, cyanosis, slow and feeble pulse, fall in body temperature, contraction of the pupil, and absence of the eye reflexes. Treatment consists of the application of warmth, administration (by means of an endo-tracheal catheter, if available) of 10 per cent. CO_2 in oxygen, and the intravenous injection of 2-3 c.c. of coramine, which is stated to be almost specific as an antidote¹⁸.

There was one death in the series of cases under review.

A. K. was admitted for removal of tonsils and adenoids. He was just thirteen years of age, but weighed 10 st. 10½ lb. and received 5.3 c.c. of avertin. The boy went to sleep in the usual way after being given avertin at 3 o'clock in the afternoon, operation taking place about 4 o'clock. At 5.45 haemorrhage occurred when he was seen by the operator and the medical superintendent. He was seen again at 7 p.m. when he was not showing the usual signs of returning consciousness. At 8 p.m. he was cyanosed and his respirations were reduced in frequency. No improvement taking place, at 9.30 oxygen and carbon dioxide were administered, and the anaesthetist was sent for, oxygen and carbon dioxide then being given by intra-tracheal catheter, and artificial respiration resorted to for half an hour with considerable improvement. The respiration rate returned to normal. He then for the first time showed signs of returning consciousness. Whilst in the theatre he had an intravenous gum saline administered with the usual cardiac and respiratory stimulants with a rectal wash-out. A liver preparation was also used. At 9.30 a.m. on the following day the pulse was good in rate and volume, the respiratory rate normal, but the patient had not recovered consciousness. Further cardiac stimulants were injected. At 11 a.m. respiration failed, and death took place at noon, twenty-one hours after the administration of avertin. At the post-mortem examination the pituitary gland showed some signs of enlargement and the pathologists's report was:—'The gland appeared to be slightly larger in size than normal. Towards one side there was a paler area, possibly of slightly firmer consistence than the rest of the gland. On microscopical examination the anterior pituitary substance was normal in appearance with no localized overgrowth of any type of cell. There is probably some degree of diffuse hyperplasia but no definite adenoma and no tuberculosis.'

The writer is indebted to Dr. J. D'Ewart, Medical Superintendent of the Booth Hall Hospital, Manchester, both for so kindly placing at his disposal all the valuable material and knowledge obtained from a study of this series of cases, and also for ever-ready help and advice in the actual preparation of this paper.

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BRITISH PAEDIATRIC ASSOCIATION

PROCEEDINGS OF THE NINTH ANNUAL GENERAL MEETING

The Ninth Annual General Meeting was held at the Old England Lake Hotel, Windermere, on Friday and Saturday, May 8th and 9th, 1936.

FIRST SESSION (MAY 8TH, 10 A.M.)

Business Proceedings: The President, Professor A. E. Naish (Sheffield), was in the Chair, and there were present 52 members.

The Minutes of the last Meeting were read and approved.

The following Officers, Honorary, Corresponding and Ordinary Members were elected:—

President: 1936-37, Dr. Leonard Findlay (London).

Secretary: Dr. A. G. Maitland-Jones (re-elected).

Treasurer: Dr. H. Morley Fletcher (re-elected).

Representative for London: Dr. W. P. H. Sheldon in place of Dr. Alan Moncrieff.

Representative for Ireland: Dr. R. Marshall (Belfast) in place of Dr. F. M. B. Allen.

Honorary Members: Dr. J. H. Thursfield (Past President) and Dr. J. S. Y. Rogers (Dundee).

Corresponding Members: Professor A. Czerny (Germany) and Dr. A. Jeffreys Wood (Australasia).

Ordinary Members: Dr. E. A. Cockayne (London), Dr. H. L. Wallace (Edinburgh) and Dr. T. Pearse Williams (London).

The Treasurer's Report was received and adopted.

It was proposed by Dr. D'Ewart, and seconded by Dr. Morley Fletcher, that a sum of ten guineas be sent to the Royal Medical Benevolent Fund, this being the centenary year of that Association. This was agreed to unanimously.

It was proposed by Dr. Robert Hutchison, and seconded by Dr. Morley Fletcher, that a Sub-Committee of the Association, consisting of Dr. N. Capon and Dr. A. Moncrieff, be set up to consider the standard of weight accepted for the definition of prematurity, this Sub-Committee to have the power to act and to co-opt with the Children's Section of the Royal Society of Medicine. This was agreed to unanimously.

The Secretary then brought to the notice of the Association a letter from the Office of the High Commissioner for India concerning the facilities for Post-Graduate Indian Students working for the Diploma of Child Health Examination.

The place of next year's meeting was then discussed, and it was decided to leave the matter in the hands of the Executive Committee.

1. DR. ALAN MONCRIEFF (London): 'Nasal obstruction in the newborn.' Several examples of this condition, bony or permanent, inflammatory or temporary, were described, and it was emphasised that during the first ten days of life a baby will not naturally breathe through the mouth, even if gross nasal obstruction is present. It was suggested that a soft rubber catheter should be passed through the nostrils in all instances where there appears to be difficulty with breathing.

2. DR. N. B. CAPON (Liverpool): 'Two cases of calcification of the suprarenal glands.' He reported two cases in which the diagnosis of suprarenal calcification was made by radiography. Neither child showed any evidence of tuberculosis, and the clinical histories indicated that in all probability the calcification was secondary to suprarenal haemorrhage during birth. This view seemed particularly probable in case 1, a girl whose age is now sixteen months and who was born by difficult breech delivery; for three days her life was in the balance but she gradually improved. Now she is in a good state of nutrition, but shows spastic diplegia. Case 2 was a girl of thirteen years who died of pneumonia following peritonitis secondary to appendicitis. The notes of her birth and early days of life were not so reliable as in case 1, but she was delivered by forceps and the labour is said to have been difficult. Unfortunately it was not possible to obtain permission for an autopsy. Brief references were made to the literature, especially to the papers of Baumann, Victor, and Snelling and Erb.

3. DR. W. BROWN (Aberdeen): 'Subnormal temperatures in infancy.' A series of 88 infants, under one year, with rectal temperatures under 98° F. was described. Of these, 58 were subnormal for long periods (days). Excluding two of the groups, cerebral (15) and prematurity (9), practically all cases in the series showed a history of malnutrition due to vomiting or refusal to feed. Inadequate caloric intake was considered to be the main cause of the low temperature, special proof of this being seen in a pyloric group (16), where the temperature rose immediately following operation or the cessation of spasm. The other 30 cases showed occasional falls, the lowest readings being noted between midnight and 4 a.m. Exposure to cold is a subsidiary factor in causation and was noted often in infants who had been taken a long motor journey in winter. All infants with a temperature below 95° should have it taken again by a low-recording thermometer: 89° F. was the lowest recorded temperature in any infant who survived. Treatment consisted of (1) adequate diet with extra glucose, and (2) the application of external heat by means of bottles, electric cage or blanket. For very low readings, below 92°, the cage is used for a short time, but has to be carefully watched; it tends to overheat the infant too quickly and to cause perspiration, resulting in no rise or even a further fall. It is preferable to use a wire cage 7½ inches high covered by a thin woollen blanket bearing the electric blanket. A self-recording thermometer is placed beside the infant and read at intervals. A three-way switch regulates the degree of heat. A temperature of over 100° F. may be reached; thus frequent inspection is necessary to keep it at the optimum of about 90° F.

4. DR. R. W. B. ELLIS (London): 'Precocious puberty and pseudohermaphroditism.' The relationship and types of these two conditions were discussed with particular reference to six illustrative cases. (1) Interuterine 'interrenalism' in a female infant, the external genitalia being of male type and the internal of female type; the ovary contained true rete testis, and the adrenals were greatly hypertrophied. (2) Pseudohermaphroditism in a female child, with precocious appearance of pubic hair and gigantism. (3) 'Infant Hercules' syndrome in a male infant aged eighteen months. (4) Precocious puberty in a male aged five, and effect of unilateral adrenalectomy. (5) Precocious puberty associated with hydrocephalus and gigantism in a boy aged three and a half. (6) Precocious

hirsutes and monstrous obesity in a female child of twelve. Reference was also made to the occurrence of precocious puberty in association with tumours of the gonads, of the floor of the third ventricle, and of the pineal body, and to the possible relationship of the two latter to the pituitary. The asymmetric appearance of male characters in the female, and of unilateral gigantism associated with precocious puberty in males, would, in certain instances, imply a chromosomal as well as an endocrine asymmetry.

5. DR. A. G. WATKINS (Cardiff): 'Spontaneous surgical emphysema.' Two cases of spontaneous surgical emphysema were described. The first a girl aged four and a half, following a spasmodic cough—not proven as whooping cough—of four days' duration developed surgical emphysema, commencing on the left side of the neck, spreading on to the face and chest wall. This was accompanied by clinical and radiographical signs of a left-sided pneumothorax. Recovery was complete. The second case, a girl aged five, developed extensive surgical emphysema from the scalp to the thighs, first noticed on the left side of the neck. This arose following three days' continuous sneezing, a whooping-cough variant. There were signs of pneumonia at the right base. Although severely ill at the onset, she gradually made a complete recovery. No surgical measures were adopted for the emphysema. A specimen of lung was shown from a boy aged four, who died thirty-six hours after the onset of a severe cough. Associated with a haemorrhagic broncho-pneumonia was interstitial emphysema, interlobar and interlobular, extending towards the hilum. This was taken to illustrate the mechanism by which the subcutaneous emphysema arose, by tracking up the hilar lymphatics and so escaping at the root of the neck.

6. DR. HUGH T. ASHBY (Manchester): 'The influence of trauma on the onset of acute poliomyelitis.' A boy aged three and a half years injured his back and fractured the right femur while sliding down a chute in a public park. He was admitted to hospital and ten days later he had a rise of temperature and pain in the right iliac fossa. This was thought to be an attack of mild appendicitis and he was operated upon. The appendix, however, was found to be normal and he soon recovered. When the splints were removed from the leg at the end of a month, the whole leg, from the buttock to the ankle, was found to be paralysed, wasted and cold. He had evidently had an attack of acute infantile paralysis while in hospital and ten days after the accident. Six months later he could only draw the leg up weakly, and he could only walk a few steps without help. It is recorded by several writers that an injury may predispose to or accelerate an attack of infantile paralysis. It was asked, if this is correct, whether the injury in this case had any connection with the infantile paralysis or not.

7. DR. LEONARD FINDLAY (London): 'Nutritional anaemia in East End of London.' He discussed the question of the incidence of nutritional anaemia as shown by examination of the children admitted under his care in the Princess Elizabeth of York Hospital for Children. Contrary to what is frequently stated, he did not find much evidence of anaemia. The haemoglobin and red cell counts showed variations within fairly wide limits, but in only comparatively few instances was the haemoglobin under 70 per cent. (Haldane standard) and the red cell count under 4,000,000 per cent. men. The average haemoglobin and red cell contents, both during infancy and childhood, followed closely the normals of various authors, and particularly closely that described by Dr. R. Hutchison in 1905.

8. DR. R. C. JEWESBURY (London): 'Intra-muscular injection of blood as a therapeutic measure.' The administration of blood is frequently resorted to therapeutically in the treatment of certain conditions, and the mode of introduction of blood is usually by transfusion. In the case of the infant whole blood is given intramuscularly with dramatic success, particularly in cases of haemorrhagic disease

of the new-born. It is a question as to how far the introduction of whole blood into an infant may be of therapeutic value in conditions other than those which are due to some obvious deficiency in the blood itself. It may be sometimes difficult or even impossible to give a blood transfusion to a wasted, anaemic infant, although special dexterity may be acquired by frequent practice. Furthermore, blood grouping is necessary before the donor's blood can be used. The intramuscular injection of whole blood is an exceedingly simple procedure—20 c.c. can be injected into the buttocks at a time, and it may be repeated at frequent intervals if necessary. The injected blood is rapidly absorbed and produces no untoward reaction. This method has been found of value in the treatment of marasmic infants in whom toxic symptoms have been a marked feature, and the results in this type of case seem to justify further trials.

SECOND SESSION (MAY 9TH, 10 A.M.).

9. DR. C. P. LAPAGE (Manchester): 'Micrognathia or hypoplasia of the mandible in the new-born.' Babies with this trouble have a tendency to attacks of cyanosis owing to the tongue falling to the back of the mouth. They are improved by turning on their faces, and may feed better in that position. Their lower jaw shows extreme smallness when attention is focused on it. Cleft palate is common. Treatment was discussed. Extreme care in feeding is necessary at first. Individual attention is important, and much can be done by teaching the baby to push its lower jaw forward with the appliance suggested by Davis and Dunn. The jaw naturally tends to come forward with the development of the lower teeth. A splint which passes round the forehead and tends to push the jaw forwards had been tried in this case without much success. Causation is possibly inter-uterine, perhaps from malposition in utero from pressure of the sternum on the chin. However, strong hereditary tendencies have been found by one author. The importance of the condition is that it may escape detection owing to lack of knowledge of its existence, and much can be done towards permanent recovery, at least in the less severe cases.

10. DR. G. B. FLEMING (Glasgow): 'The blood-sugar in convulsions.' The changes in the level of the blood-sugar in forty children with convulsions were described. The ages of the patients varied from two days to eleven years, and the convulsions were due to various causes:—birth injury, meningitis, spasmodophilia, and epilepsy. The blood-sugar during or immediately after the first of a series of convulsions was found in many cases to be raised and gradually fell to low levels. This state of hypoglycaemia lasted for many hours and was not influenced by taking food. It is suggested that the initial hyperglycaemia is due to the cerebral disturbance acting on the suprarenals producing mobilization of glycogen into glucose. The subsequent hypoglycaemia is probably not due to exhaustion of carbohydrate stores in the body, as the ingestion of food containing carbohydrate did not raise the blood-sugar level, but to exhaustion of adrenaline. Against the first hypothesis and in favour of the latter is the observation that, in two cases, injection of adrenaline caused a temporary rise in the blood-sugar level. It is concluded that the disturbance in the carbohydrate metabolism which occurs in convulsions due to various conditions is the result and not the cause of the cerebral disturbance.

11. DR. C. WALLACE ROSS (Birmingham), introduced by PROF. L. G. PARSONS: 'The carbohydrate metabolism in abdominal tuberculosis.' Two types were described. First, in cases in which the glandular lesions were predominant, flat oral glucose tolerance curves were found to be associated with high intravenous ones. Upon this evidence, together with a state of relative insensitivity to injected insulin, the speaker based his belief that there is a defective power to

absorb carbohydrate in these cases. Secondly, in a case in which ascites was prominent, but without conspicuous glandular enlargement, a different condition was found, a high intravenous result being associated with a high oral one. This was presumed to be due to a toxic state of the patient, of which there was striking clinical evidence. In both types of case the relative intolerance for glucose was presumed to be due to a shortage of 'insulinkinase,' and results were quoted showing that this substance could apparently be supplied, with restoration of tolerance towards normal, either by the injection of campolon intravenously or by the giving of liquid extract of liver by mouth. This had been used in treatment with encouraging results.

12. DR. N. MORRIS (Glasgow): 'The treatment of diabetes mellitus in childhood.' A summary was given of the experiences at the Diabetic Clinic of the Royal Hospital for Sick Children, Glasgow, during the past ten years. Of forty-two patients eleven (26.2 per cent.) have died, seven with coma, two with generalized tuberculosis, and two with infectious diseases. No significant difference was noted in the average protein intake per kgm. or insulin per kgm. in the surviving and fatal cases, but in the former the total caloric intake and the percentage of calories as carbohydrate were greater. In the survivors both physical and mental development were good. The effect of increasing the dietary carbohydrate was tested in a group of fourteen patients: of these ten required more total insulin and eight more insulin per kgm. body weight, while six utilized less carbohydrate per unit of insulin. The aims of treatment are to maintain a sense of general well-being and to keep the urine acetone-free and, if possible, sugar-free. The diet is fixed at a level to satisfy each child: a satisfactory first approximation of the dietary requirements is obtained by adding 50 per cent. to the basal figures of Benedict and Talbot. The amount of carbohydrate is left to the child's choice, but a free diet has been found to be unsatisfactory. In some patients seasonal variations in insulin requirements were noted, less being necessary in the summer months.

13. DR. B. SCHLESINGER (London): 'Treatment of enteritis by apple diet.' After describing the method of preparing the apples, the mode of administration and the transitional diet which it was necessary for the child to have before resuming his normal meals, he discussed the type of case in which most benefit was obtained. Infants under one year were not generally suitable, but the treatment appeared to be equally effective in all acute types of infection. Some of his cases had been severe examples of bacillary dysentery with fever, great shock, vomiting and innumerable stools containing large quantities of blood and mucus. The patients were thoroughly ill and seemed to recover more rapidly with apple diet than other similar cases had in his experience with the more usual methods of treatment. There was no guarantee, however, against the continued presence of dysentery bacilli in the stools, although the patients themselves seemed to have recovered.

14. DR. G. H. NEWNS AND DR. R. WILSON (London), introduced by DR. D. PATERSON: 'The treatment of pyelitis in children by mandelic acid.' Thirty-five cases treated with mandelic acid at the Hospital for Sick Children, Great Ormond Street, and Westminster Hospital were reported. The majority were girls over two years. In thirty cases the infection was due to *B.coli*. Five cases showed evidence of kidney damage or renal tract abnormality, the remaining having apparently straightforward pyelitis. Mandelic acid (with sodium bicarbonate) was used in most cases. The dose varied from 60 to 120 grains daily according to the age of the child. Ammonium chloride, in doses of about half the above, was given to make the urine acid. Neocit (a powdered preparation of mandelic acid and sodium bicarbonate) was used in six cases. This obviated the necessity of

giving ammonium chloride. This preparation did not, however, maintain the pH of the urine constantly at the necessary low level. A pH of 5.6 is necessary for the maximum bacteriocidal action of the mandelic acid to be obtained. No toxic effects on the kidney were observed in any of the cases. In thirty-two cases, the urine was rendered sterile, in many within a few days. This result was obtained in nine cases in which potassium citrate had been previously given without effect. The patients had urinary examinations periodically after discharge. Ten cases were found to have relapsed. Half of these may be ascribed to renal abnormalities or a non-B.coli infection. Mandelic acid appears to be an effective agent for rendering the urine sterile in cases of pyelitis. The tendency to recurrence might be minimized by more prolonged treatment.

15. DR. J. H. EBBS (Birmingham), introduced by PROF. L. G. PARSONS: 'A clinical syndrome associated with cerebral sinus thrombosis.' Twenty-one cases of cerebral sinus thrombosis were reviewed briefly and two cases described in detail, both females, aged sixteen months and two years respectively, the outstanding points being a sudden onset with restlessness, followed by convulsions; localization of the convulsions as shown by twitching and followed by paresis; marked and persistent drowsiness; the cerebro-spinal fluid findings of increased pressure, normal number of cells, cultures sterile, low sugar content, chloride values of 774 mgm. per cent. in one case, and 932 mgm. per cent. in the other, raised protein; the absence of any clinical evidence of infection; and at post mortem, thrombosis of the cerebral vessels. The chloride value of 932 mgm. per cent. in the cerebro-spinal fluid is the highest value in the records of the Birmingham Children's Hospital, and has not yet been explained. The cases represent two unusual examples of cerebral sinus thrombosis in children which have probably resulted from some remote infection.

MENINGITIS IN THE NEWBORN

BY

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Infection constitutes the most serious threat to survival with which the newborn infant has to contend. It may involve superficial or deep structures and frequently gives rise to septicaemia. In the present paper an account is given of the clinical and pathological features of twenty-one cases of neonatal meningitis (with special reference to the importance of morbid conditions of the skin and surface mucous membranes as primary foci of infection) occurring in the Royal Maternity Hospital, Edinburgh, during the past four years. Observations were made and recorded in connection with twenty of these infants from the time of birth in the course of routine clinical duties. One child, born at home, first came under observation after admission to hospital on the third day of life. Post-mortem examination was carried out in eighteen cases; in the other three cases permission for autopsy was not obtained and diagnosis was based upon the results of examination of cerebrospinal fluids obtained during life.

Clinical and pathological records.

Obstetrical details.—Of the twenty-one cases included in the series six were born at term, seven were four weeks and eight more than six weeks premature. Delivery was instrumental in one case and spontaneous in the remaining twenty which included four breech presentations. Meconium was passed in the course of four labours. There was a history of antenatal toxæmia in the case of four, and of a morbid puerperium in two mothers.

Clinical observations.—The dominating characteristics of the clinical picture were lack of desire for fluids, increasing bodily weakness and a stationary or falling weight. Other features were pronounced in only a limited number of infants. The picture was complicated by the presence of pneumonia in six and severe gastro-intestinal disturbance in two cases; atelectasis was present in a large number. A tentative diagnosis of meningitis was made during life in thirteen cases, in three of which the condition was thought to be intracranial haemorrhage prior to the examination of spinal fluid. The presence of an intracranial abnormality was not suspected in seven cases.

The condition of seventeen of the twenty-one infants was unsatisfactory at birth; four were severely asphyxiated and the remainder very feeble.

These infants never rallied satisfactorily. Their weight failed to increase after the initial physiological loss; in the smallest infants it remained stationary throughout life, in others it showed a persistent gradual decline (fig. 1, 2 and 3). Slow progressive wasting was characteristic. Typical

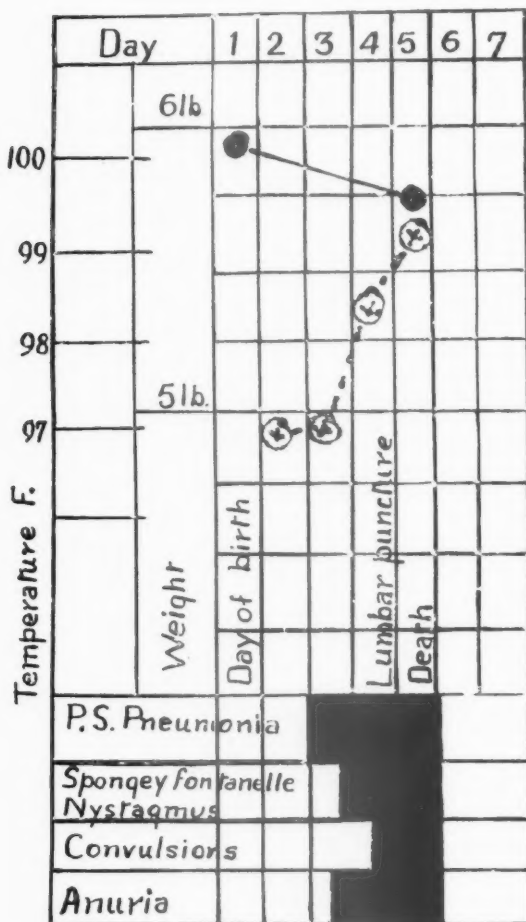
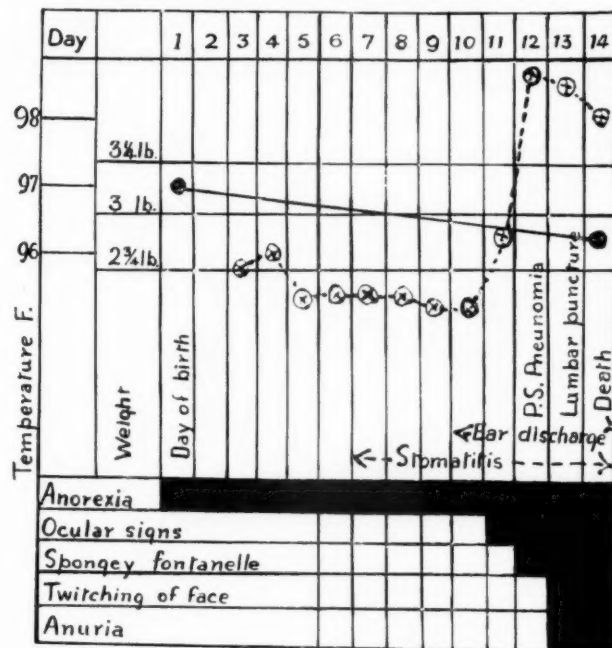


FIG. 1.—Baby C.; three weeks premature, spontaneous delivery; asphyxiated at birth. Physical signs of pneumonia present on the third day of life. Diagnosis of meningitis confirmed by lumbar puncture on the fourth day and death on the fifth day of life. Pneumonia, pulmonary abscesses and extensive meningitis (*b. coli*) present at autopsy.

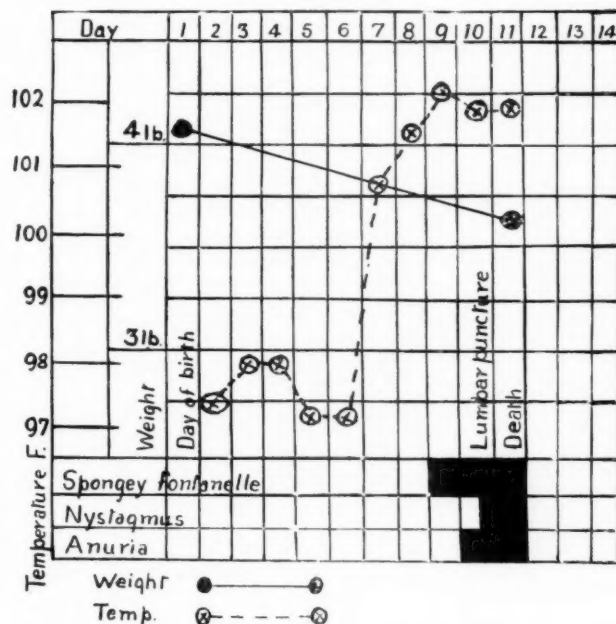
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Hippocratic facies developed in some cases. In a few an expression of great anxiety was associated with continual restless movements of the head; in two there was repeated, darting protrusion of the tongue; the picture was one of great mental restlessness associated with extreme physical weakness. Ocular signs were among the early evidences of intracranial irritation; they included inequality of the pupils, gross muscular inco-ordination in a few, and, more commonly, fine lateral nystagmus. Tendon reflexes showed no constant changes; they were exaggerated in the presence of signs of cerebral irritation but diminished in the majority of instances. General convulsions occurred in two infants in whom Babinski's sign and nuchal rigidity had been



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FIG. 2.—Baby R.; four weeks premature; spontaneous delivery; condition poor at birth; b. coli cultured during life from aural discharge and mouth; lumbar puncture on thirteenth day of life confirmed diagnosis of meningitis. Death on fourteenth day. At autopsy extensive meningitis (b. coli), bilateral otitis media, stomatitis, pneumonia.



Weight ● — ●
Temp. ⊗ — — — ⊗

FIG. 3.—Baby S.; seven weeks premature; spontaneous delivery; poor condition at birth; lumbar puncture after appearance of ocular signs on tenth day of life confirmed diagnosis of meningitis. Extensive meningitis at autopsy (b. coli).

previously observed; they were preceded by a shrill cry, were followed by a period of coma and recurred immediately before death. Localized twitching of the extremities or face, or both, occurred in eight infants; unilateral facial palsy subsequently developed in two, a right ptosis in one and slight spasticity of the limbs in four. In nine cases a spongy sensation was appreciated on palpation of the fontanelle; this was due to fullness rather than to increased tension. Vomiting was recorded in only one infant and was not projectile. Curious movements involving the upper limbs were a feature of two cases; in one they consisted of a persistent fine tremor of the hands and in the other were suggestive of ataxia. The pulse tended to increase in rate but became imperceptible and made observations in connection with it unreliable. Three infants showed no fever (fig. 4). In the other

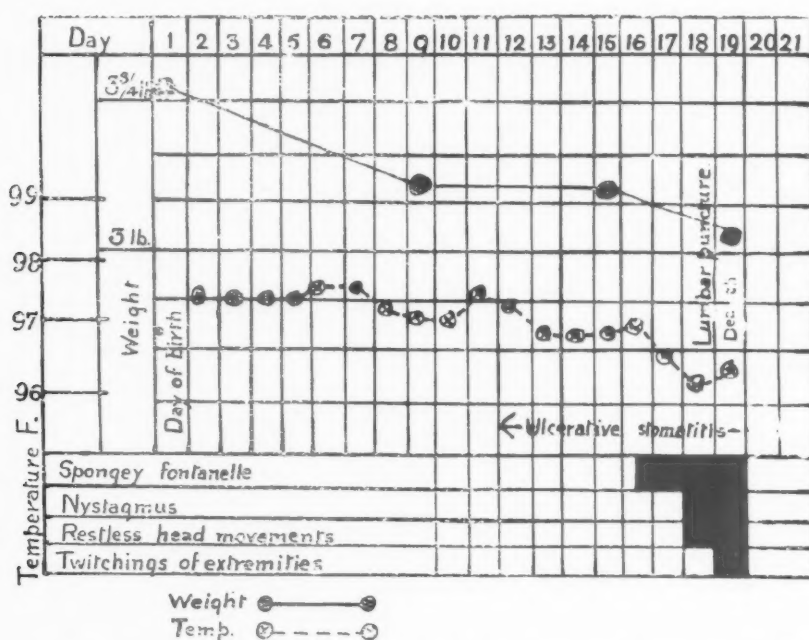


FIG. 4.—Baby L.; six weeks premature; poor condition at birth; lumbar puncture after appearance of ocular signs and evidence of mental restlessness confirmed diagnosis of meningitis. Note unusual afebrile course. Meningitis very extensive at autopsy; streptococcus cultured from c.s.f. taken during life and from smear from meninges taken at autopsy.

cases the temperature was subnormal for some time after birth but rose with remarkable constancy two to four days before death, reaching a maximum exceeding 102° F. in only one instance: it fell slightly during the last few hours of life. In two cases death was preceded by convulsions and in the others followed a short period of semi-coma. Failure to excrete urine was a feature of the terminal stages. The duration of life varied from four to twenty days; seven infants died in each of the first three weeks of life. Lumbar puncture was carried out during life in eight infants. The results of the examination of the fluids are given in table 1.

TABLE 1.
CEREBROSPINAL FLUIDS OBTAINED DURING LIFE: RESULTS OF EXAMINATION.

CASE	ORGANISMS	PRESSURE	NAKED-EYE APPEARANCE	MICROSCOPIC FINDINGS	BIOCHEMICAL FINDINGS MGM. PER 100 CC.		
					PROTEIN	SUGAR	CHLORIDES
190	B. coli ...	Decreased	Yellowish-green	Cells 400 per c.mm.—almost entirely polymorphs. Organisms intra- and extra-cellular.	200	43	650
213	B. coli ...	Normal	Yellowish-green. Very thick.	Cells mainly polymorphs. Occasional r.b.c. (probably traumatic). Organisms mainly extra-cellular.	900	16	715
206	Pneumococcus ...	Normal	Green: thick. Early fibrinous deposit.	Cells 300 per c.mm.—entirely polymorphs. Numerous organisms intra- and extra-cellular.	100	34	650
14	B. coli. Streptococcus viridans.	Decreased	Yellowish-green	Polymorphs and lymphocytes present in proportion 3:1. No organisms seen.	90	34	712
210	Staphylococcus aureus ...	Normal	Yellow: thick. Early fibrinous deposit.	Cells almost entirely polymorphs. Few r.b.c. (probably traumatic). Numerous organisms.	400	34	678
110	Streptococcus viridans ...	Normal	Green ...	Cells entirely polymorphs: 200 per c.mm. Organisms present.	100	40	—
111	B. coli ...	Decreased	Yellowish-green	Cells mainly polymorphs. 600 per c.mm. Organisms intra- and extra-cellular: numerous.	300	—	—
84	B. coli ...	Normal	Yellowish-green: thick.	Cells numerous—polymorphs. Organisms sparse, extra-cellular.	110	40	650

CASE	CLINICAL FINDINGS.			PATHOLOGICAL			
	MENINGITIS	DURATION OF LIFE (DAYS)	ASSOCIATED MORBID CONDITIONS	MENINGEAL EXUDATE			
209	Tentative diagnosis made 48 hours before death.	10	Purulent conjunctivitis with corneal ulceration.	Thick : patchy, yellow : mainly basal but also over vertex.			
210	Diagnosed	15	Dorsal meningo-myelocoele.	Thick : yellow : base of brain and spinal meninges.			
241	Tentative diagnosis made 48 hours before death.	14	Ulcerative stomatitis. Purulent nasal discharge. Cellulitis of scalp.	Massive : greenish yellow : covering entire brain.			
214	Tentative diagnosis made on day of death.	7	Dermatitis. Aural discharge.	Patchy : greenish yellow : mainly basal but also over vertex.			
212	Not suspected	11	Subcutaneous abscess ...	Thick : bright yellow : mainly basal but also related to parietal surface.			
211	Not suspected	20	Pneumonia	Thick : green : limited to under surfaces of temporal and frontal lobes.			
110	Tentative diagnosis of intraventricular haemorrhage, revised following lumbar puncture.	6	Pneumonia	Massive : related to all external cerebral surfaces.			
190	Diagnosis confirmed by lumbar puncture.	11	Pneumonia ? Peritonitis.	Massive : greenish yellow : related to all external cerebral surfaces.			
213	Diagnosis confirmed by lumbar puncture.	4	Pneumonia	Thick : green : localized to base of brain.			
235	Intracranial condition suspected.	17	—	Thick : greenish yellow : limited to lateral fissures and under surface of temporal lobe.			
125	Not suspected	16	Pneumonia	Massive : yellow : mainly basal and involving all surfaces of pons and cerebellum.			
143	Tentative diagnosis made 36 hours before death.	11	Ulcerative stomatitis ...	Massive : greenish yellow : mainly basal involving pons and cerebellum.			
205	Not suspected	15	Aural discharge (bilateral)	Sparse—in thin, small patches, limited to under surface of occipital lobe : green.			
206	Diagnosis confirmed by lumbar puncture.	4	Purulent nasal discharge	Patchy, but extensive and thick : related to all external surfaces of cerebrum : green.			
207	Not suspected	12	Ulcerative stomatitis. Acute intestinal disturbance.	Moderately thick : greenish yellow : limited to under surface right temporal lobe.			
208	Not suspected	7	Extensive pustular skin condition. Pneumonia.	Thin : greenish yellow : limited to lateral surface of left parietal lobe.			
243	Not suspected	8	Pneumonia. Purulent nasal discharge.	Sparse : greenish yellow : limited to the under surface of the occipital lobe.			
251	Intraventricular haemorrhage suspected : diagnosis revised following lumbar puncture.	19	—	Thick : green : mainly basal.			
111	Intraventricular haemorrhage suspected : diagnosis revised following lumbar puncture.	14	Cellulitis of scalp ...	No autopsy			
84	Diagnosis confirmed by lumbar puncture.	6	Acute alimentary disturbance. Infection of cephalohaematoma.	No autopsy			
14	Diagnosis confirmed by lumbar puncture.	20	—	No autopsy			

* From material obtained during life.

LE 2.

21 CASES OF NEONATAL MENINGITIS.

FINDINGS		BACTERIOLOGICAL FINDINGS.	
ASSOCIATED CONDITIONS		CULTURE OF C.S.F. OR FROM MENINGEAL EXUDATE	VARIOUS.
Corneal ulceration		Staphylococcus aureus... ..	Eye*—Staphylococcus aureus.
Spina bifida : meningomyelocele		*Staphylococcus aureus... ..	Blood—Staphylococcus aureus. B. coli.
Stomatitis. Cellulitis of scalp ...		B. coli.	Pus from scalp*—B. coli.
Bilateral otitis media		Staphylococcus aureus. B. coli	Ear*—Staphylococcus aureus, pneumococcus.
—		B. coli /	Skin—Staphylococcus aureus. Blood—B. coli. Subcutaneous abscess.*—B. coli.
Pneumonia		Atypical coliform organism of the salmonella group.†	Blood.—Atypical coliform organism of the salmonella group.†
Thrombosis of the straight sinus. Pneumonia with pleurisy. Pericarditis. Suprarenal haemorrhage. Pneumonia		*Streptococcus viridans	—
Peritonitis.		*B. coli	Blood.—B. coli.
Pneumonia		*B. coli	Mouth*—B. coli. Blood.—B. coli.
Haemorrhage into kidney ...		B. coli	—
Pneumonia. Secondary haemorrhage into cerebellum from septic thrombus.		Staphylococcus aureus. B. coli.	—
Stomatitis. Thrombosis of chorioidal veins with secondary intraventricular haemorrhage.		B. coli	—
Bilateral otitis media		Haemolytic streptococcus. Staphylococcus aureus. B.coli.	Aural discharge.*—Haemolytic streptococci. Blood.—Staphylococcus aureus. Blood.—B. coli.
—		*Pneumococcus	
Stomatitis... ..		B. coli	Mouth.*—B. coli.
Ulcerative colitis.			Stools.*—No departure from normal intestinal flora.
Pneumonia		Staphylococcus aureus ...	Lung abscess.—Staphylococcus aureus. Blood.—Staphylococcus aureus.
Pericarditis. Lung abscess. Pneumonia		B. coli	Nose.*—B. coli. Mouth.*—B. coli. Ear.—B. coli. Meninges.—B. coli.
Bilateral otitis media.			
—		*Streptococcus viridans ...	—
—		*B. coli	Scalp*.—B. coli.
—		*B. coli	Stools*.—No departure from normal intestinal flora. Cephalohaematoma*—aspirated pus—B. coli.
—		*Streptococci viridans. B. coli.	—

† See appendix (p. 185).

Infection of the skin, mucous membranes or subcutaneous tissues was a common finding. In one infant pustules developed over the entire body on the second day of life and disappeared several days before death: in another the appearance of extensive dermatitis preceded death by five days. Ulcerative stomatitis was a feature of four cases: in one there was purulent conjunctivitis with ulceration of the cornea and purulent discharge was noted from the nose in three, and from the ears in two cases. Localized cellulitis of the scalp arose from infection of a superficial forcep's abrasion in one case and of a laceration resulting from the application of Willet's forceps in another: in a third there was secondary infection of a cephalohaematoma. Meningitis followed the development of sepsis in a large dorsal meningomyelocoele in one child. Examination of the urine in sixteen cases showed nothing abnormal.

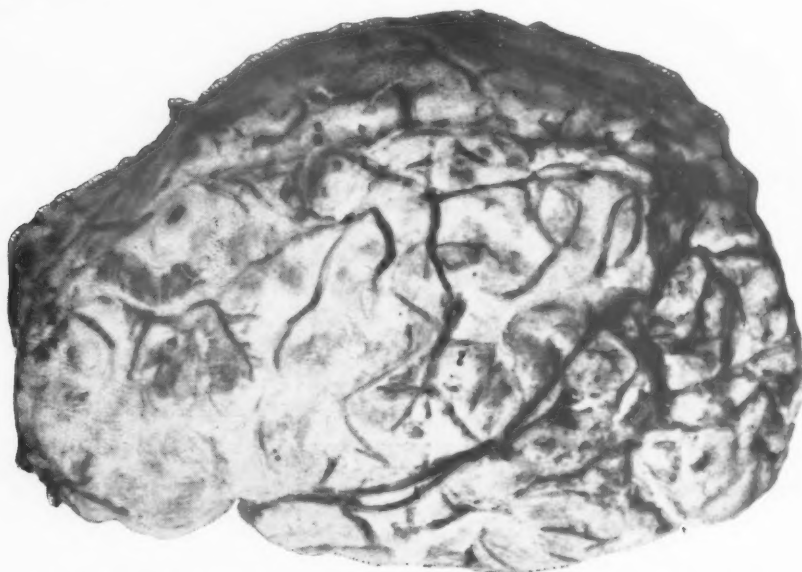


FIG. 5.—Baby S.; *b. coli* meningitis in infant dying on eleventh day of life, showing thick inflammatory deposit extending over the whole of the lateral surfaces of the cerebrum. Signs suggestive of meningitis did not appear until two days before death.

Pathological findings.—The extent of the inflammatory exudate varied. In some cases there was a thin deposit along the lines of the meningeal vessels; in others a thick exudate was limited to the base of the brain and the lateral fissures; in a few a massive purulent deposit extended uniformly from the vertex to base (fig. 5) and involved the surfaces of mid-brain and cerebellum. Intense generalized congestion of the meninges was characteristic even in cases where the inflammatory deposit was strictly localized. The choroid plexus was covered in a number of cases, and the ventricular walls in a few instances with exudate similar in nature to that on the surface of the brain. Abundant exudate was sometimes accompanied by flattening of the cerebral convolutions over the vertex. In two of the three cases in which the cord was examined there was involvement of the spinal meninges.

Microscopically the meningeal exudate presented the usual features (fig. 6). Organisms were present in large numbers and in advanced cases phagocytosis of polymorphonuclear cells by macrophages was evident. The amount of fibrin present varied. Apart from the occurrence of intracerebellar haemorrhage in one case (see below) changes in the brain substance were limited to slight congestion and oedema.

Associated conditions found at autopsy included pneumonia in seven, pericarditis in two, ulcerative colitis in one, peritonitis in one and otitis media in three infants. Pneumonia had developed around pulmonary

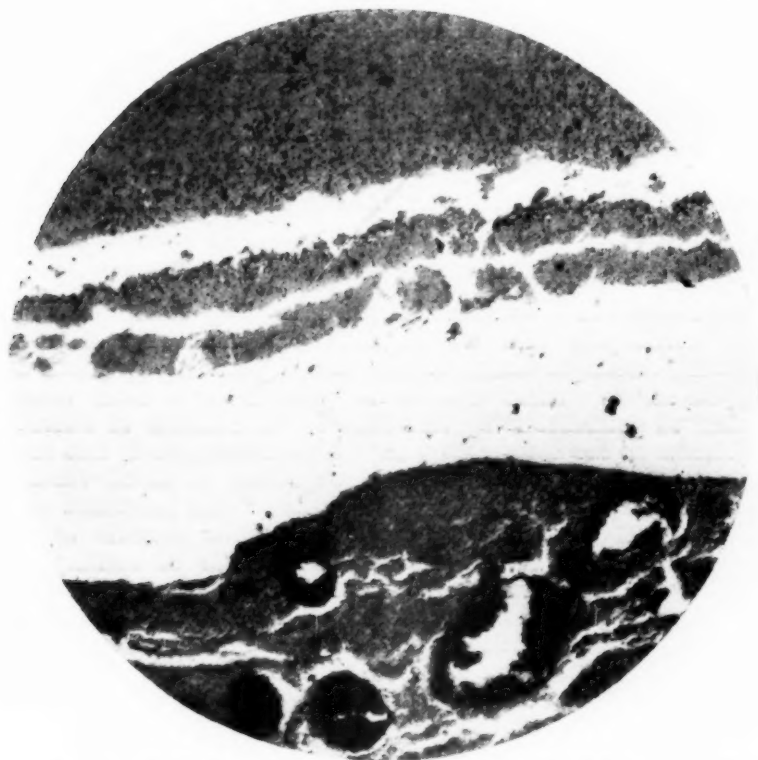


FIG. 6.—Baby L. Thick exudate (cells and fibrin) in a case of pneumococcal meningitis dying on the fourth day of life. There is severe congestion of the brain substance. Symptoms suggestive of an intra-cranial condition did not appear until within eighteen hours of death.

abscesses in one case and was associated with empyema in another. Atelectasis of varying extent was present in the majority of cases.

Haemorrhage arising from thrombosed vessels was present in three cases. In one the cerebral ventricular system was filled with blood arising from the veins of the chorioid plexus; in another extensive subdural haemorrhage had followed thrombosis of the straight sinus; and in the third case localized haemorrhage had taken place into the medullary substance of the cerebellum.

Bacteriological findings.—These are given in table 2. A pure culture of *b. coli* was grown from the meninges or spinal fluid in ten cases: in three mixed growths included *b. coli*. In one case meningitis was due to infection by an atypical organism of the *Salmonella* group and in the remainder to infection by the common pyogenic organisms.

Discussion.

Eighteen of the twenty-one cases of the present series came to autopsy; they represent almost 8 per cent. of the two hundred and thirty post-mortem examinations carried out on newborn infants by the writer during the period of this study. Cruickshank¹¹ found meningitis in 4 per cent. of eight hundred cases of neonatal death. His thirty-three cases of meningitis included fourteen premature infants (42 per cent.): in the present series there were fifteen premature infants or 71 per cent. of the total of twenty-one cases. The differences between the two series indicate the care with which general conclusions must be arrived at in the study of a limited number of cases. A review of the more important observations made in connection with neonatal meningitis by various workers gives some indication of the many factors which may give rise to these differences.

The condition has been attributed to many organisms. Barron⁴ found records of meningitis due to *b. coli*, streptococcus, staphylococcus, pneumococcus, meningococcus, *b. mucosus capsulatus*, *b. lactis aerogenes* and *b. pyocyaneus*. Cases due to *b. proteus* have been described by Cathala⁷ and to gonococcus by Bradford⁸. A number of observers have drawn attention to the frequency with which meningitis is due to infection by *b. coli*. Cruickshank¹¹ found this organism in more than half the autopsies on twenty-three infants and Gibbens¹³ has described three cases which came to autopsy within a period of twelve months in a London hospital. Scherer²³ was of the opinion that cases of meningitis due to *b. coli* in newborn infants occurred with greater frequency in hospital during periods of overcrowding. In explanation of the high incidence of this form of meningitis Cooke and Bell⁶ argue that there is decreased resistance to bacterial infection as the result of the absence of 'the normal agglutinins for *b. coli*' in the newborn; they also refer to the greater permeability of the intestinal mucosa at that age and stress the influence of digestive disturbance.

The pathological findings recorded by a number of writers indicate that meningitis is frequently the result of generalized septicaemia and Fothergill and Sweet¹² isolated *b. coli* during life from the blood and spinal fluid of several cases of meningitis in the newborn.

The time at which infection occurs varies and may be related to antenatal, natal or postnatal factors. Athenstaedt² describes a case of *b. coli* septicaemia involving the meninges in a newborn infant in which he considers transplacental transmission of infection from a maternal pyelitis took place. Hinsdale¹⁶ records a case in which neonatal meningitis followed umbilical infection derived from an intrauterine collection of pus. Infection is attributed to the introduction of a finger into the infant's mouth during labour in a case described by Barron⁴. Goldreich¹⁴ reports a fourth case in which meningitis was present at autopsy on the second day of life, having given rise to symptoms during the previous twenty-four hours; he considers that infection was antenatal, was favoured by a long dry labour and was was aspirated into the lungs.

Infection has been attributed to aspiration of infected liquor amnii by Aschoff³ and Herrman¹⁵ among others. This mode of infection has been emphasized by Browne⁶ in connection with neonatal pneumonia. Pulmonary infection may result in septicaemia and subsequent meningitis but, as Cruickshank¹¹ remarks, difficulty exists in determining whether the pneumonia is a primary or a secondary factor. The alimentary and urinary tracts are suggested as possible portals of entry for infection by Gibbens¹³ and Herrman¹⁵.

There are several references in the literature to the association of otitis media with meningitis in the newborn. It is probable that in these cases infection of the meninges was a result of direct spread from the ear. In two cases recorded by Cruickshank¹¹ *b. coli* was cultured from both the meninges and the ears. The occurrence of otitis media in the newborn is attributed by Aschoff³ to the passage of infected liquor amnii along the eustachian tubes as a result of efforts at premature respiration. Scherer²³ suggests that otitis media may follow the lodgment of infected bath water in the ear.

Observers agree regarding the difficulty in diagnosing meningitis in newborn infants. The condition was not suspected during life in a large number of the recorded cases. Gibbens¹³ explains the frequent absence of evidence of increased intracranial pressure by the ability of the skull of the newborn infant to adapt itself within certain limits to increase in the volume of its contents. The same author agrees also with the view expressed by Koplik¹⁷ that meningitis may be confused with tetany. Ravid²⁰ points out that meningitis may be indicated by the least specific signs; in this connection he considers that the condition is nearly always ushered in by gastro-intestinal disturbance and attaches importance to distension of the veins of the neck and to dissociation of the pulse rate and temperature. He describes fever as irregular in these cases: von Reuss²¹ is of the opinion that it may be entirely absent or very insignificant, and stresses a tense, bulging fontanelle and convulsions as among the most helpful points in diagnosis: he considers the late appearance of convulsions of value in differentiating the condition from birth trauma. An unusual case of recovery from *b. coli* meningitis is recorded by Neff¹⁹, but it is significant that the question of treatment receives no attention in the literature.

Present series.—In the present series it was not always possible to determine whether extension of the infection to the meninges had been direct or by the blood stream, but the pathological and bacteriological findings leave little doubt that primary foci of infection were present in the skin (two cases), the tissues of the scalp (two cases), and the eyes (one case). Pathological evidence of septicaemia was present in ten cases, in six of which confirmation was obtained as a result of bacteriological examination of autopsy material. The presence of ulcerative colitis suggests that infection of the blood may have occurred in the intestine in one case. Considering the frequency with which primary foci are demonstrable in other situations alimentary infection must necessarily be rare, and little significance can be attached to gastro-intestinal symptoms as evidence of the mode of infection. Infection of the blood may have occurred in the lungs of the seven infants in which pneumonia was present. In four of these cases superficial septic foci appeared a considerable time before signs and symptoms suggestive of pneumonia, and it is probable that in these cases pulmonary lesions were secondary manifestations of a generalized septicaemia.

There was no evidence of urinary infection in any of the cases under discussion. In a series of sixty-one cases of urinary infection in the newborn the present writer¹⁰ found no evidence of meningitis: the great majority of such cases recover. It may be assumed from these facts that meningitis rarely results from a primary infection of the urinary tract.

In three cases meningitis was the result of direct extension of infection from the ear. In two of these cases infection was present in the bucco-nasal cavities and the otitis media is probably explained by the passage of organisms along the eustachian tube. The third case may be explained in the same way despite the absence of any obvious focus of infection as Aries¹ has drawn attention to the frequent presence of organisms in the mouths of apparently healthy newborn infants. The view expressed by Leathart¹⁸ would suggest that the supine position in which these debilitated infants were fed was a factor favouring extension of infection in the way described. These facts show that in discussing neonatal meningitis the same importance is to be attached to infections of the upper respiratory passages as of the skin, eye and scalp as potential primary foci of infection.

Meningitis of the newborn due to an organism of the *Salmonella* group has not been previously recorded. In other respects the bacteriological findings in the present series do not differ from those mentioned by earlier writers. A feature of the cases under discussion was the frequency with which the *b. coli* was responsible for infection of the superficial tissues. This observation suggests that the large number of cases of neonatal meningitis due to *b. coli* is largely accounted for by the many risks of exposure to infection by that organism peculiar to newborn infants.

The appearance of the meningeal exudate gave no clue as to the nature of the casual organism but its distribution explained certain clinical features. The absence of classical signs of meningitis was accounted for in several infants by the sparse nature of the inflammatory exudate. In other infants the clinical signs were those of cranial nerve involvement and were explained by the localization of the meningeal deposit over the base of the brain. This was a feature of a number of autopsies and explained the infrequency with which cortical irritation gave rise to convulsive movements.

The explanation given by Gibbens¹³ for the absence of signs arising from increased intracranial pressure finds support in two observations made in connection with the present series. In the first place there were symptoms of increased intracranial pressure in only two cases: they appeared abruptly, were rapidly followed by death and at autopsy were explained by gross intracranial haemorrhage complicating meningitis. In these cases it may be assumed that the skull was unable to adapt itself to the sudden massive increase in the bulk of its contents resulting from haemorrhage. In the second place, the findings reported here confirm the views held by von Reuss²¹ that meningitis is particularly liable to occur in premature infants. The loose nature of the membranes connecting the bones of the skull in these infants would appear to indicate that the theory advanced by Gibbens has a special application in their case. It is possible therefore that the predominance of

premature infants in cases of neonatal meningitis seen in the present series accounts for the infrequency with which symptoms of increased intracranial pressure appear.

The frequent absence of classical signs makes the diagnosis of meningitis in the newborn difficult. It is important to remember the possibility of the condition and to note the existence of predisposing factors. Chief among these are prematurity and the presence of infection. Both of these factors were present in fifteen of the cases under discussion. Meningitis is particularly liable to occur where sepsis develops in a premature infant whose clinical course since birth has been characterized by a falling or stationary weight curve and by slowly increasing physical weakness. Neonatal pneumonia has to be considered in the differential diagnosis and difficulty may arise from the combined presence of pneumonia and meningitis as seen in six cases of this series. As already described by the present writer⁹ the existence of pneumonia is suggested by attacks of slight cyanosis which disappear with the administration of oxygen and can usually be confirmed by auscultatory findings.

Signs of intracranial disturbance occurring after the first week of life should always suggest meningitis. They were characteristic of over 66 per cent. of our cases. The clinical signs which proved of greatest value in the present series were ocular inco-ordination and nystagmus, especially when associated with an expression of fear or with restless movements of the head. Importance was always attached to 'sponginess' of the fontanelle. Intraventricular haemorrhage is frequently associated with the late appearance of similar features but they are more abrupt in onset, severer in nature and accompanied by signs of more acute general distress: the fontanelle bulges and is tense, the cry is shriller and convulsive movements of the limbs are grosser than in cases of meningitis. In both conditions death is usually preceded by a rise in temperature but whereas in cases of meningitis it is present for two to four days (fig. 1 and 3), it is a strictly terminal event in intraventricular haemorrhage.

Lumbar puncture is essential for a final diagnosis. The presence of meningitis is suggested by the colour and the turbidity of the fluid obtained and can be rapidly confirmed by microscopical examination. The results of biochemical examination of the few specimens of spinal fluid obtained, did not differ from those recorded in similar cases occurring in older children.

The case of partial recovery described by Neff¹⁹ must be considered a rare exception. Treatment of the developed condition is limited to the amelioration of symptoms and preventive measures are the only ones which can influence the neonatal death rate due to meningitis. Prevention depends upon the elimination of the risks of infection to which infants are exposed in the neonatal period.

In any study of meningitis the source and the mode of infection are points of primary importance. Many views have been advanced in this connection in discussions dealing with the condition in the newborn. Observations made on cases included in the present series reveal the

importance of morbid conditions of the skin and surface mucous membranes as primary foci of infection. In the majority of cases infection of these structures was not evident for a considerable time after birth and was probably derived from the mother, the attendants or, in the case of infants not on the breast, from the feeds. Surface infections appearing during the first few days of life may have been derived from similar sources or acquired during labour from infected liquor amnii or the external genitalia.

The risks attached to morbid conditions of the skin and mucous membranes in the newborn is not sufficiently appreciated. Prevention depends upon meticulous attention to the hygiene of the skin, mouth, eyes, nasal passages and external auditory meati. Abrasions of the skin and catarrh of the mucous membranes must be considered as potential dangers. Unremitting attention to hygiene should begin with the birth of the child.

Summary.

1. Clinical observations from the time of birth are described in connection with twenty-one cases of meningitis in newborn infants. Details are given of the findings at eighteen autopsies. The results of bacteriological examination of specimens obtained during life and at post-mortem examination are recorded.

2. Meningitis is usually part of a generalized septicaemia but it is not always possible to determine whether infection of the meninges has been by the blood stream or as the result of direct extension from other foci.

3. The bacteriology of meningitis differs in the newborn from that found in older subjects. Neonatal meningitis is frequently the result of *b. coli* infection; occasionally it results from infection by organisms of comparative rarity. In the twenty-one cases described *b. coli* was the causal organism in approximately half that number; in one infant meningitis resulted from septicaemia due to an atypical organism of the *Salmonella* group.

4. Morbid conditions of the skin, subcutaneous tissues or surface mucous membranes were present in fifteen cases. Their presence, especially in premature infants, constitutes a definite risk of meningitis.

5. Infection of the mouth and nasal passages is associated with special risks on account of the ease with which extension may occur along the eustachian tubes and give rise to otitis media and subsequent meningitis.

6. Neonatal meningitis cannot always be diagnosed. The classical signs of meningitis are often absent. Importance is attached to prematurity and the presence of infection as predisposing factors. Signs of intracranial disturbance occurring after the first week of life should always suggest meningitis; of these ocular signs, sponginess of the fontanelle, and mental restlessness are the most common. Fever of a few days' duration usually precedes death. Convulsions are rare. The condition has to be differentiated from pneumonia in afebrile cases, and from intra-ventricular haemorrhage in the presence of signs arising from increased intracranial pressure. Lumbar puncture is essential for a final diagnosis.

7. Neonatal meningitis illustrates the seriousness of the threat to survival in infection of the newborn. The skin and surface mucous membranes are common portals of entry for infection. The danger of infection can be greatly lessened by meticulous attention to the hygiene of the skin, mouth, eyes, nasal passages and external auditory meati. This care should commence with the birth of the infant.

Thanks must be expressed to Prof. Charles McNeil and to Prof. R. W. Johnstone for their advice and encouragement; to Dr. A. R. Macgregor for the majority of the bacteriological reports; and to Col. W. F. Harvey, Col. Glen Liston and Dr. W. D. Kermack, all of the Laboratory of the Royal College of Physicians, Edinburgh, for various investigations in connection with specimens of cerebro-spinal fluid. Dr. C. P. Beattie must also be thanked for reports in connection with the bacteriology of one case.

Appendix.

Dr. C. P. Beattie, of the University Bacteriological Department, Edinburgh, carried out investigations in connection with the organism found in case No. 211 (table 2). He reported as follows:—

The organism was a gram negative, non-motile bacillus. The non-motility of the organism was a considerable bar to its identification as it was impossible to make use of 'H' antigens. It remained non-motile in spite of frequent subcultures in broth. The sugar reactions were glucose positive, lactose negative, dulcitol positive, saccharose negative, mannitol positive, xylose positive, inositol negative, glycerine negative, adonitol negative, arabinose positive, raffinose negative, salicin negative, rhamnose positive, lead acetate agar—blackened, indol negative, Voges-Proskauer negative, gelatin—not liquefied.

The organism was tested against representative sera of the various 'O' groups with the following results:—

ORGANISM.	GROUP.	TITRE.
Paratyphosus A	VI	6,400
Paratyphosus B	I, II	1:400
Gaertner	III	1:3200
Suipestifer	V	0
Newport	IV	0
"L"	VII	0

The organism if of the Salmonella group appeared to have 'O' antigen III or VI or both.

The absorption test showed it not to be 'paratyphosus A' or B. enteritidis Gaertner. The organisms with the same 'O' as Para. A. is Newcastle. With this the organism gave only a low titre agglutination. In view of the sugar reactions and serological test the organism may have been a non-motile variant of Dar-es-Salaam, Eastbourne or Tokyo. On the other hand, it more probably belonged to a strain not previously identified.

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PARENTAL LOSS AND CHILD GUIDANCE

BY

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The personality development of a child depends to a considerable extent upon the influence of those who surround it in its early days, and principally upon the influences of its father and its mother. While this development may be adversely affected by circumstances in the relationships in normally constituted family life, nevertheless, the normal state may be considered as one in which both parents are exerting their separate and combined influences. During the routine investigation of 'Child Guidance' cases, interest was aroused by the relative prevalence of some variation from the normal parental constitution, and this led to an inquiry into what part such a factor played in the etiology of behaviour and nervous disorders in childhood. It was, therefore, decided to study a consecutive series of unselected cases already dealt with at the Liverpool and District Child Guidance Clinic, and to collect the information relating to the parental state for the purpose of discovering the relative frequency with which there was some disturbance in the normal parental relationship and its influence, if any, on the children and their individual problems.

The following facts were recorded and tabulated. The sex of the child; the age of the child; the problem on account of which the child was referred to the Clinic; the intellectual development, as assessed by the Clinic staff; the agency through which the case was referred; the actual position as regards the presence and residence of the parents in the home at the time of reference. The total number of cases investigated was 484. Of this number 266 were, at the time of reference, living in normal homes, that is, homes in which the child's own father and mother were present. The remaining 218 cases, 45 per cent. of the total, came from what are described as disturbed homes, that is, homes from which one or both parents were missing.

Results of Analysis.

In table 1 the cases under review are considered, first, with regard to the difference in sex in the two groups; secondly, with regard to the difference in age, the ages being divided into pre-school, elementary school,

TABLE 1.

					NORMAL HOMES		DISTURBED HOMES		TOTAL OF BOTH	
					Total	Per Cent.	Total	Per Cent.	Total	Per Cent.
SEX										
Male	164	61	109	50	273	56
Female	102	39	109	50	211	44
AGE										
Under 5 years	28	10½	7	3	35	7
5 to 14 years	202	76	165	76	367	76
Over 14 years	36	13½	46	21	82	17
PROBLEM ON REFERENCE										
Behaviour	113	42	118	54	231	48
Nervous	103	39	52	24	155	32
Educational	32	12	17	8	49	10
Mixed Problems	18	7	31	14	49	10
INTELLIGENCE										
Very Superior	4	1½	1	—	5	1
Superior	25	9	20	9	45	9½
Average	90	34	81	37	171	37½
Inferior	73	27½	73	34	146	30
Very Inferior	19	7	16	7½	35	7
Not taken	55	21	27	12½	82	17
SOURCE										
Educational	136	51	92	42	228	47
Medical	69	26	29	13	98	20
Institutions, Social Agencies, Courts	39	15	71	33	110	23
Others	22	8	26	12	48	10

and post-elementary school, for the purpose; thirdly, the problem on reference was sub-divided into four categories, according to whether behaviour symptoms, nervous symptoms, or educational symptoms pre-

dominated, the mixed problem group being reserved for those cases in which there was more than one type of problem, but none predominated; fourthly, intelligence capacity was graded according to the intelligence quotients, where these had been estimated, as follows: average intelligence includes I.Qs between 90 and 110, superior between 110 and 130, and very superior above 130, inferior between 90 and 70, and very inferior below 70; fifthly, an effort has been made to classify the source of reference in such a way as to indicate clearly any possible bias in the origin of cases.

The totals column of table 1 records certain statistical data of a consecutive series of cases dealt with at the Liverpool and District Child Guidance Clinic, and may be of interest to Child Guidance Clinics in other areas. It will be seen that more boys than girls are treated, in the proportion of five to four, and that three-quarters of the cases are of elementary school age. Unsatisfactory behaviour is complained of in 48 per cent. of the cases, and nervous symptoms account for 32 per cent. The figures relating to intelligence capacity might suggest that some retardation of intellect is a factor in the genesis of the disorders dealt with, but it should be noted that in eighty-two cases, or 17 per cent., estimation of intellect was not carried out, the commonest reason for such omission being that it was considered from scholastic or other information that the patient was of at least average intellect, or that intellectual capacity had no bearing on the problem under consideration.

That 47 per cent. of the patients were referred from educational sources, indicates that the troubles for which the Clinic was consulted had most frequently been detected through educational channels, although the great majority of this number were notified to the Clinic by school medical officers. The 20 per cent. of the patients who come from purely medical sources were from general practitioners and consultants, and had in the first place sought medical advice. The third group (institutions, social agencies, etc.), was segregated on account of any possible moral bias or likelihood of unusual parentage. 'Others' include those referred from various sources in insignificant numbers, e.g., parents, private persons, etc.

The main interest of this investigation is to consider, under the same headings, the facts disclosed in a comparison of cases from normal and from disturbed homes. These facts are set down in columns 1 and 2, and the points that appear to be worthy of comment are as follows:—

From normal homes boys are more frequently seen than girls, in the proportion of three to two, while from the disturbed homes the sexes are equal in number. Children of elementary school age equal 76 per cent. in both groups, but, as might be expected, there is a slight increase in the number of older children and a proportionate decrease in pre-school children from homes where one or both parents are absent. Behaviour and nervous disorders accounted for four-fifths of the problems for which the Clinic was consulted, and

from normal homes the numbers of each type were approximately equal. The cases from disturbed homes, however, were predominantly of the former kind, more than twice as many being referred for behaviour troubles as for nervous. The assessments of intellectual capacity approximate closely in both columns, an observation of considerable interest in view of the possibility of an unfavourable heredity in many of the disturbed-home cases and the general expectation of mental inferiority in circumstances such as illegitimacy.

The comparison of these two groups would not be complete without some consideration of the sources of reference of the cases. Children who have suffered the loss of one or both parents are frequently under the supervision of welfare societies or similar social agencies, or have been placed in institutions or homes, and it is natural that this group would show an increase in reference from such sources. Nevertheless, it is to be noted that the numbers referred from educational bodies approximate fairly closely in both groups. It has been mentioned that 218 of our patients came from homes where they lacked the influence of the normal father-mother relationship. Consideration of this generalization leads to a subdivision of these cases into three groups.

1. PARENTAL LOSS.

Cases in which one or both parents were lost	139
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2. TEMPORARY PARENTAL LOSS.

Cases in which one or both parents were absent from the						
home intermittently	33

3. CASES OF ILLEGITIMATE BIRTH	46
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These groups are analysed separately under the same headings as in table 1, with the results shown in table 2. Here it will be seen that the sex ratios in these three groups are approximately equal, and that the age periods show no appreciable variation. The prevalence of behaviour disorder is seen to persist in each group, most marked in the illegitimate children, and less so in the cases with temporary parental loss. Intelligence capacity shows no falling off in the illegitimate group where the percentages approximate to the average for the whole series of Child Guidance cases. The largest percentage of cases in the illegitimate group was from social agencies, institutions, etc., while from homes where parents are temporarily absent there is an increased number sent by the medical profession.

An investigation has been made into the causes of parental loss, together with an analysis of the status of those on whom had lain the onus of guardianship at the time of reference, as follows:—

PARENTAL LOSS—139 cases.

<i>Cause of loss :</i>	<i>Father.</i>	<i>Mother.</i>	<i>Total.</i>
Death	50	59	109
Divorce, desertion, separation ...	31	11	42
Illness or occupation	12	7	19
	—	—	—
	93	77	170
	—	—	—

TABLE 2

	PARENTAL LOSS		TEMPORARY PARENTAL LOSS		ILLEGITIMATE		TOTALS	
	Total	Per cent.	Total	Per cent.	Total	Per cent.	Total	Per cent.
SEX								
Male	72	52	16	48½	21	46	109	50
Female	67	48	17	51½	25	54	109	50
AGE								
Under 5 years ...	2	1	3	9	2	4	7	3
5 to 14 years ...	107	77	23	70	35	76	165	76
Over 14 years ...	30	22	7	21	9	20	46	21
PROBLEM ON REFERRAL								
Behaviour	74	53	16	48½	28	61	118	54
Nervous	34	24	11	33½	7	15	52	24
Educational	12	9	2	6	3	7	17	8
Mixed problems...	19	14	4	12	8	17	31	14
INTELLIGENCE								
Very superior ...	—	—	1	3	—	—	1	—
Superior	7	5	9	27½	4	9	20	9
Average	53	38	10	30½	18	39	81	37
Inferior	48	35	8	24	17	37	73	34
Very inferior ...	13	9	3	9	—	—	16	7½
Not taken	18	13	2	6	7	15	27	12½
SOURCE								
Educational	66	47	12	36½	14	30½	92	42
Medical	12	9	11	33½	6	13	29	13
Institutions, social agencies, courts	44	32	7	21	20	43½	71	33
Others	17	12	3	9	6	13	26	12

On the nineteen occasions on which parents were lost to their children by illness or occupation, this loss was occasioned by detention in mental hospitals or other institutions, or by employment abroad.

METHOD OF REPLACEMENT.

<i>Group</i>		<i>Replaced by :</i>	
Both parents lost	...	Relatives	15
31 cases	...	Adoptive parents	8
		Institutions	4
		Foster parents	3
		Step-mother	1
Father only lost	...	Not replaced	39
62 cases	...	Step-father	10
		Relatives	10
		Institutions	3
Mother only lost	...	Step-mother	25
46 cases	...	Not replaced	8
		Institutions	7
		Relatives	5
		Foster-mother	1

TEMPORARY PARENTAL LOSS: 33 cases.—In twenty-eight of this small group one or other of the parents had been periodically absent from the home on account of occupation or illness, so that the children did not have, in effect, the normal dual parental influence. In nineteen of the cases the fathers were seafaring, in seven they were commercial travellers or were following similar occupations. Chronic illness, with interrupted institutional treatment, accounted for two cases. In addition to these there were five instances in which children had normal homes, but were temporarily resident in Training Homes or Approved Schools.

CASES OF ILLEGITIMATE BIRTH: 46 cases.—In this group, while in some cases much is known of the parentage, the information, as a general rule, is too inconsistent and unreliable to be of value. The present interest is the ascertainment of the guardianship under which the child is being brought up, and these facts are as follows :—

Mother and step-father	13
Homes and institutions	12
Adoptive or foster parents	8
Maternal relatives	4
Mother and maternal grandparents	3
Own parents, unmarried	3
Mother only	2
Step-father and his family	1

Although the three cases in which the illegitimate children were living with their own, but unmarried, parents, do not really belong to the disturbed home series, it was decided to include them with the main group of illegitimate cases rather than with the normal home cases.

Observations.

Although comparative figures for the community as a whole are not available, the fact that forty-five per cent. of the cases investigated showed some disturbance of the normal family grouping suggested that this factor is an important one in the work of Child Guidance. It may be contended that this high proportion is the result of the way in which Child Guidance cases are selected. Many are under the supervision of social agencies or institutions from whom assistance is readily sought by the guardians, and readily given, and such agencies are usually conversant with the existence and objects of child guidance work. Consideration of the sources of reference shows that there is some justification for this view, but yet insufficient to give a complete explanation.

In comparing the children from disturbed homes with those from normal homes, the findings with regard to sex incidence suggests that whereas in the normal home the average girl tends to identify herself with the home and, therefore, to conform to the wishes of her parents without the display of nervous or behaviour symptoms, there is a lack of security in the environment of the disturbed home which affects the children, regardless of their sex. The fact that behaviour disorders are more prevalent from disturbed homes is considered to be attributable, firstly, to the fact of faulty handling through the absence of parents or presence of substitute parents and, secondly, to the fact that in many cases comparatively mild forms of behaviour disturbance which would be understood by the child's own parents are less readily tolerated by the substitute parents. The uniformity of intellectual development in the two series suggests that the environmental aspects of the disturbed home problem are of more significance than the inherent factors, otherwise greater evidence of inferiority would be expected among these cases. Much fuller information regarding hereditary factors would, however, be required before any definite statement could be made upon this subject.

An inquiry into the way in which parents had been lost to their children supplied no information other than might have been anticipated, except perhaps for the fact that 33 per cent. of the fathers were lost to their children through divorce, separation or desertion, all of which situations might be expected to produce an adverse emotional situation in the home and to react unfavourably upon the children on this account. In the question of the replacement of parents, the commonest situation was one in which the father was not replaced, leaving the mother with the sole responsibility of the upbringing of her children. On the other hand, where the mother was lost, the father tended to re-marry, and by doing so created the step-parent situation, which is admittedly a difficult one both for parent and for child.

Conclusions.

Reviewing the position as a whole it is concluded that the child from the disturbed home differs as to personality in no ascertainable way from the child from the normal home, but that there are circumstances in the

disturbed home environment and possibilities of difficulty or stress for the child which may lead to the production of symptoms. In a consideration of the problem of the disturbed, or what has come to be known as the broken home, however, this cannot be regarded as a single entity, but as a medley of facts and circumstances, decisive in their origin, but diffuse in their manifestations and extensive in their effects. Foremost is the tragedy of the loss through death and the deprivation of moral support, and possibly of economic stability, which the remaining parent may have to face. More complicated is the case of the orphaned child, while illegitimacy brings with it an entirely new set of difficulties both for the child and for its guardians. Incompatibility in the parents, as evidenced by divorce, legal separation and desertion, implies an adverse emotional situation, while seafaring and similar occupations are apt to contribute specific difficulties. Unfavourable influences may be present to produce disorder in the child from the normal home, but the child from the disturbed home is required to adapt himself to environmental circumstances presenting added difficulties, with increased possibilities for maladjustment. He lacks the influence of the balanced father-mother relationship; parent substitutes rarely possess that quality of sympathy which normally exists between parents and offspring; there may be the absence of unity of control which obtains when multiple guardians attempt to rear the child, or he may be subjected to the restricting influences of institutional life.

The facts revealed by this investigation emphasize the necessity for a study of the environmental situation in Child Guidance work. The repressive, punitive or symptomatic methods of dealing with these cases may have their successes, but the future well-being and efficiency of the individual is best cared for when the environment is studied in relation to the personality. A realization of the environmental situation by parent, child and doctor is often the first step to overcoming the nervous and behaviour disorders of childhood.

Thanks are due to Miss D. E. Brown, B.Sc. (Econ.) for her ready help in the task of scrutinizing the case papers and collecting and tabulating much of the material used in this investigation.

STAPHYLOCOCCAL PNEUMONIA

BY

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That cases of pneumonia occur in which staphylococcus is the sole, or the predominating, infecting micro-organism is well known. Many of the reported cases have been associated with epidemics of influenza. Although generally less frequent than streptococcus haemolyticus and Pfeiffer's bacillus as a cause of pneumonia complicating influenza, staphylococcus aureus has been conspicuous in certain epidemics. Chickering and Park¹ described one of these and noted the very grave and often fatal character of the pneumonia when staphylococcus aureus played a leading role. In such cases it is to be supposed that the staphylococcus is a secondary invader, following upon the epidemic infection which has laid the respiratory tract open to attack. Apart from these occasional epidemics, staphylococcal pneumonia appears to be relatively uncommon. It may be questioned, therefore, whether staphylococcus ever causes pneumonia independently of other micro-organisms, and whether those cases in which it plays a dominant part have clinical or pathological features sufficiently distinctive to justify this condition being regarded as an entity, differing from other forms of broncho-pneumonia. Reimann², in a paper describing six cases, claims 'primary staphylococcic pneumonia' as a clinical and pathological entity. The facts now recorded from a series of ten fatal cases support this claim at least to the extent that they show this type of pneumonia to possess certain constant and distinctive features.

Case reports.

The ten cases were encountered in the pathological department of the Royal Edinburgh Hospital for Sick Children between August, 1935, and May, 1936. During that period there was no influenza epidemic of any serious proportions in the community, and in the hospital the incidence of pneumonia in general, though fairly high during the winter, was not unusual. But the occurrence of so many cases of staphylococcal infection of the lungs (other than pyaemic) within so comparatively short a time is without precedent in the records of the department.

For purposes of description the ten cases may be divided into two groups, according to the stage at which the pathological process was found at necropsy: (1) Four cases with sero-fibrinous pleural effusion, in which the early stages of the process in the lungs were shown; (2) six

cases with empyema or pyo-pneumothorax, in which the pathological process in the lungs had progressed to a later stage.

Group I. Case 1. A boy, aged seven weeks, was an under-weight, bottle-fed baby. The fatal illness was of four days' duration, with restlessness, slight fever (99.4° F.) and cough. On admission to hospital on the third day, physical signs indicated consolidation of the right lung.

POST-MORTEM EXAMINATION The right pleural cavity contained one ounce of thin turbid fluid and fibrinous exudate; there were numerous sub-pleural haemorrhages. The upper lobe of the right lung was completely consolidated, haemorrhagic and moist. The bronchi in this part contained much thick pus. The other lobes were not consolidated. There was no generalized bronchitis. The left lung and pleura were healthy.

BACTERIOLOGY. *Staphylococcus aureus* was obtained in pure culture, post-mortem, from lung, pleural fluid and blood.

Case 2 was that of a girl aged four months. She had had bronchitis two weeks before admission to hospital, but had made a good recovery. The fatal illness was of three days' duration and began with a cough, sneezing, nasal discharge and restlessness, followed by respiratory distress. When admitted to hospital on the third day the infant was cyanosed and very ill. Physical signs indicated consolidation in the left upper and right lower lobes. The temperature was 105.4° F.; the white blood cells numbered 31,000 per c.mm.

POST-MORTEM EXAMINATION. Both pleural cavities contained a quantity of slightly turbid serous fluid and fibrinous exudate; there were many sub-pleural haemorrhages. There were large well-defined areas of consolidation in the left upper and both lower lobes; all these were haemorrhagic, with yellow points of suppuration showing through the pleura, and blood-stained pus exuded from the cut surface. Other parts were not consolidated and there was no generalized bronchitis.

BACTERIOLOGY. *Staphylococcus aureus* was obtained in pure culture, post-mortem, from lung, pleural exudate and blood.

Case 3 was that of a boy aged three-and-a-half years. He had always been healthy. The fatal illness was of eight hours' duration. He appeared to be quite well in the morning. At noon he asked to be put to bed. He became obviously ill during the afternoon; vomited blood at 6 p.m. and again an hour later; and died at 8 p.m. on the way to hospital.

POST-MORTEM EXAMINATION. Both pleural sacs contained one ounce of slightly turbid blood-stained fluid and fibrinous exudate; there were many sub-pleural haemorrhages. The left lower lobe and the base of the right lower lobe were consolidated and very haemorrhagic. There was no pneumonia elsewhere, and no generalized bronchitis. The pharynx and larynx were inflamed.

BACTERIOLOGY. *Staphylococcus aureus* was obtained in pure culture from lung and pleural exudate. Blood culture yielded a pure growth of pneumococcus Type II. All cultures were made post-mortem.

Case 4 was that of a girl aged sixteen days, born prematurely by one-and-a-half months and illegitimate. She was feeble and would not take the breast; she was fed with breast milk from a bottle. The fatal illness was of about twenty hours' duration. She refused feeds and was pale and collapsed; blood came from the nose and a black motion was passed. She was moribund when admitted to hospital.

POST-MORTEM EXAMINATION. The right pleural cavity was full of blood-stained serous fluid; copious sub-pleural haemorrhage made the whole serous membrane crimson. There was a small patch of consolidation at the apex of the right upper lobe, sharply defined, haemorrhagic. The rest of the right lung was collapsed. The left pleural sac and lung were healthy. There was no generalized bronchitis. The upper respiratory passages were not inflamed. The ileum contained altered blood.

BACTERIOLOGY. *Staphylococcus aureus* was obtained in pure culture, post-mortem, from the right lung, pleural exudate and blood.

The macroscopic characters of these four cases were so similar and so unlike other types of pneumonia that each one, after the first, was recognized at necropsy and tentatively diagnosed as staphylococcal pneumonia before any bacteriological investigation had been carried out. In each there was a pleural effusion of sero-fibrinous fluid, slightly turbid or

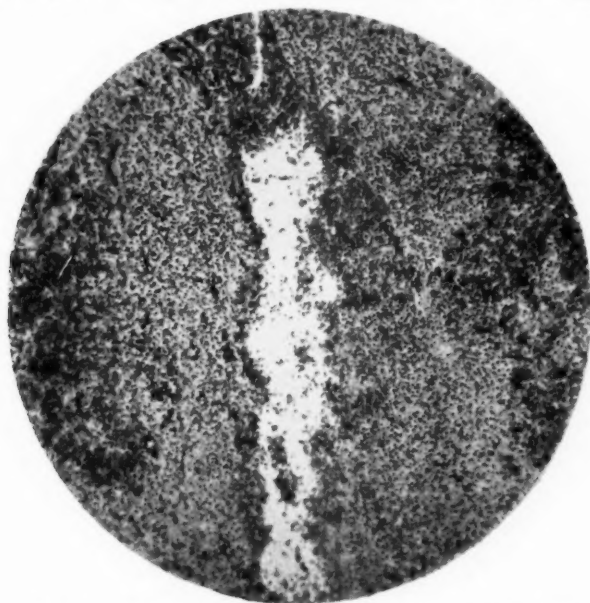


FIG. 1. Case 3. A bronchus with early suppuration destroying the wall, surrounded by haemorrhagic consolidation (x 60)

blood-stained, with numerous sub-pleural haemorrhages. Each had one or more areas of massive consolidation, sharply defined, intensely haemorrhagic, with a soft, moist surface on section which suggested the early onset of suppuration. In each there was an absence of generalized bronchitis and of scattered small patches of consolidation such as are found in the usual forms of broncho-pneumonia. In no case was any focus of infection found to which the pneumonia might have been secondary, nor were there any pyaemic lesions. The other organs showed the usual toxic changes, which were always severe.

The microscopic characters of these four cases were so similar that separate description is unnecessary. The consolidation was due to a combination of haemorrhage and inflammatory exudation. The haemorrhage affected both the alveoli and the coarse stroma. The exudate was

cellular in alveoli and bronchi, with heavy deposits of fibrin in the interlobular septa. Even in the earliest cases there was a strong tendency to suppuration, which might develop anywhere, but especially in the bronchi (see fig. 1), where the walls were destroyed and adjacent alveoli were involved; and in interlobular septa and perivascular stroma, where it spread along, and out from, the lymph vessels. Throughout the affected parts there were extraordinary numbers of staphylococci in large clumps (see fig. 2). Other parts of the lungs showed no pathological changes except some congestion and oedema.

Group II. Case 5 was that of a boy aged ten weeks. He was a feeble baby and had been losing weight; there had been an umbilical discharge. The fatal illness was of ten days' duration and began with a sudden rise of temperature to 103.4° F. and consolidation in the left lung. On the day before death 40 c.c. of pus was removed from the left pleural cavity.

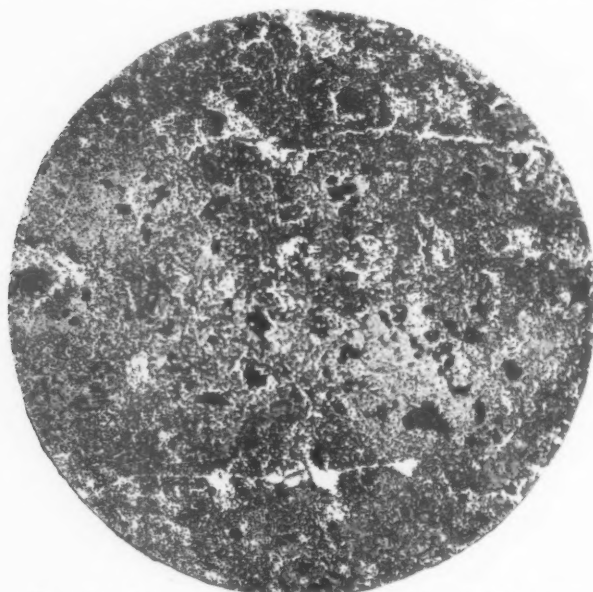


FIG. 2. Case 4. Masses of staphylococci among haemorrhagic and purulent exudate (x 55)

POST-MORTEM EXAMINATION. The left pleural sac showed organized adhesions anteriorly, and posteriorly contained a large quantity of pus. There was a small area of suppuration in the left lung near the base of the lower lobe, from which pus was discharging into the pleural cavity. The rest of the left lung was collapsed. There was no generalized bronchitis. The right lung and pleura were healthy.

BACTERIOLOGY. *Staphylococcus aureus* was obtained in pure culture from the pleural pus during life.

Case 6 was that of a boy aged one year. The fatal illness was of three days' duration, with fever (105° F.), cough, dyspnoea and blood-stained discharge from the nose. He was moribund when admitted to hospital.

POST-MORTEM EXAMINATION. The right pleural cavity contained thin pus and fibrino-purulent exudate. At the anterior border of the right upper lobe a consolidated area of about two cubic inches contained many

ramifying abscesses, several of which had burst through the pleura. The rest of the right lung was collapsed. The left lung and pleura were healthy. The pharynx and tonsils were inflamed.

BACTERIOLOGY. A strongly haemolytic strain of staphylococcus albus was obtained in pure culture from pleural pus removed just before death.

Case 7 was that of a girl aged four months. The fatal illness was of thirty-six hours' duration, but was preceded by a slight cold and cough for a few days. She became pale and collapsed, with respiratory distress and fever (103° F.).

POST-MORTEM EXAMINATION. The right pleural cavity contained a large amount of thin pus and air. A consolidated area of about three-quarters of a cubic inch at the base of the right lower lobe was riddled with ramifying abscesses, one of which had burst through the pleura. The rest of the right lung was collapsed. The left lung and pleura were healthy. There was early fibrinous pericarditis.

BACTERIOLOGY. Staphylococcus aureus was obtained in pure culture, post-mortem, from the pleural pus, but in direct films other organisms also were present, notably streptococci and Gram-negative diplococci of the Neisseria group.

Case 8 was that of a boy aged four months. The fatal illness was of five days' duration, with dyspnoea, cyanosis and fever (104.2° F.). The white blood cells numbered 26,000 per c.mm.

POST-MORTEM EXAMINATION. The left pleural cavity contained a large quantity of thin pus, fibrino-purulent exudate and air. A consolidated area at the base of the left lower lobe was riddled with ramifying abscesses, one of which had burst through the pleura. The rest of the left lung was collapsed. There was broncho-pneumonia without sup-puration at the base of the right lung.

BACTERIOLOGY. Staphylococcus aureus and pneumococcus were obtained from the pleural pus during life.

Case 9 was that of a boy aged six months. The fatal illness was of twenty-five days' duration, with pallor, panting, cough and sweating. During a feed (cows' milk) he had choked and from that moment there was increasing respiratory distress. He was treated at home, where he developed pneumonia in the left lung. On the fourteenth day he became worse, and on the eighteenth day he was admitted to hospital with an empyema. Skiagrams showed a pyo-pneumothorax, and fifty cc. of pus and air were evacuated from the left pleural cavity. Staphylococcal antitoxin (B.W. & Co.) was given, ten cc. by the intravenous and ten cc. by the intramuscular route over forty-eight hours, with temporary improvement. Death followed a sudden collapse.

POST-MORTEM EXAMINATION. The left pleural cavity was mostly obliterated by fibrous adhesions, among which were several pockets of thick pus. The antero-inferior portion of the left upper lobe was riddled with ramifying abscesses, several of which had burst through the pleura. The rest of the left lung was collapsed. The right lung and pleura were healthy.

BACTERIOLOGY. Staphylococcus aureus was obtained in pure culture from the pleural pus and blood during life and from the left lung after death.

Case 10 was that of a boy aged seven months. The fatal illness was of two weeks' duration, but had been preceded by measles and bronchitis from which he had never fully recovered. The symptoms of acute illness were cough, dyspnoea and cyanosis. When admitted to hospital, two days before death, his temperature was 101.8° F., and signs of fluid were present at the right base. Forty-five cc. of pus were evacuated from the right pleural cavity.

POST-MORTEM EXAMINATION. The right pleural cavity contained a large amount of pus and fibrino-purulent exudate. An area of about one cubic inch, just below the apex of the right upper lobe, was consolidated and contained ramifying abscesses, one of which had burst through the pleura. The rest of the right lung was collapsed. The left lung and pleura were healthy. The pharynx was inflamed.



FIG. 3. Case 10. Multiple abscesses in an area of haemorrhagic consolidation (x 7)

BACTERIOLOGY. *Staphylococcus aureus* and *B. influenzae*, the former predominating, were found in the pleural pus during life. After death, *staphylococcus aureus* was obtained in pure culture from the right lung, and *streptococcus haemolyticus* from the blood.

The remarkable similarity of the pathological findings in these six cases cannot fail to be noted. Every case had a unilateral empyema; in three cases there was a pyo-pneumothorax. In every case suppuration had developed in the corresponding lung in a localized area which was never very large and often quite small. Within the affected area in every case multiple ramifying abscesses had formed, one or more of which had burst through the pleura. In all except case 8 there was an absence of generalized bronchitis and of consolidation in either lung apart from the single area involved in suppuration. Case 8, in which there was a mixed infection, showed broncho-pneumonia in the base of the other lung.

The microscopic characters were almost identical in the six cases. In all but one the abscesses were of an acute type, without evidence of any organization. The exception was case 5, in which some of the cavities had a lining membrane of recent granulation tissue. In many instances some of the cavities were bounded in part by fragments of bronchial wall, or had a traceable connection with bronchi. Sometimes suppuration had originated in lymph vessels in the interlobular septa. Although acute, the abscesses were usually fairly sharply defined. The lung substance between them was collapsed or consolidated, and only occasionally showed spreading necrosis and suppuration. (see fig. 3 and 4.)



FIG. 4. Case 5. Well defined abscess cavities separated by collapsed lung substance (x 5)

It is obvious that these six cases illustrate a further stage of the pathological process seen in its earlier stage in cases 1 to 4. Both groups show the same localization of the lung lesion to certain well-defined areas, and the same absence of generalized bronchitis and of the disseminated patches of consolidation so constantly found in broncho-pneumonia due to other organisms. The incipient suppuration arising especially, though not only, in the bronchi, which was noted in the cases of group I, had developed in those of group II into a series of ramifying abscess cavities, rupture of which through the pleura had produced empyema. When this happens, if the almost inevitable broncho-pleural fistula communicates with a bronchus which still contains air, pyo-pneumothorax will result, as in cases 7, 8 and 9.

Bacteriological summary.

In nine of the ten cases staphylococcus aureus was isolated, and in one case staphylococcus albus. In six cases no evidence was obtained from the bacteriological investigation that any micro-organisms other than staphylococcus played any part. In cases 7, 8 and 10, although staphylococcus predominated, other organisms accompanied it in the lung or pleural exudate, viz., streptococcus and a coccus of the Neisseria group in case 7, pneumococcus in case 8, and B. influenzae in case 10, in which there was also a haemolytic streptococcus in the blood. In Cases 7 and 10 there was a definite history of a respiratory infection preceding the onset of the fatal illness. In case 8, while no such history was obtained, in addition to the characteristic staphylococcal lesion, there was, in the other lung, an acute broncho-pneumonia without suppuration, which may have been due to the pneumococcus. In these three cases, therefore, it is likely that the staphylococcal infection was superimposed on a previous respiratory infection of another type. In case 3, that rather extraordinary case of a previously healthy boy who died within eight hours of the onset of symptoms, while as far as could be ascertained staphylococcus aureus was responsible for the pulmonary condition, there was a coincident pneumococcal septicaemia. It is difficult to explain how this double infection may have arisen, but clearly it was a peculiarly deadly combination.

Discussion.

It is reasonably certain that the pathological process in the lungs in these ten cases was the result of a primary infection of the respiratory tract, and not of a haematogenous infection from a distant septic focus. In only one case was any antecedent septic focus known to exist (the umbilicus in case 5), and even there no connection was established. Study of the pathological anatomy of the lung lesion leaves little doubt that it is the result of infection which reaches the lung via the bronchi. The intimate relation of many of the abscesses to bronchi, and the severe purulent inflammation of the bronchial walls, even in the earliest cases, together with the absence of septic thrombosis of the pulmonary arteries, are features which almost prove the bronchial and disprove the vascular route. Anatomically the lesions are unlike those of pyaemic infection.

In four cases there was reason to suppose that an antecedent respiratory infection may have predisposed the lungs to attack by staphylococci. In the other six cases, although an antecedent or coincident infection by other organisms cannot be altogether ruled out, there was no evidence that staphylococcus was not alone responsible. In one

case (case 9) there was a strong suggestion in the history that the illness may have been initiated by the baby aspirating milk into the lung. Although there was no suggestive history in any other case, aspiration of food is a possibility, especially in cases 1 and 4, these patients having been feeble, premature babies who did not suck well. Milk often contains staphylococci, and it was noted by Johnson and Meyer³ that staphylococcal pneumonia in newborn infants might be caused by aspiration of food. But it is probably unnecessary always to seek the cause in any such accidental introduction of staphylococci into the lungs. As with other organisms more commonly associated with respiratory infection, their invasion of the lungs may depend upon predisposition or lowered resistance in the host, or upon their own exalted virulence. The occurrence of so many of these cases in this hospital within a relatively short period possibly indicates a phase of increased virulence among staphylococci. No statistical proof can be produced in support of this suggestion, but surgeons and pathologists working in the same city endorse the opinion that there has been in recent months an increased prevalence of other staphylococcal diseases.

Whether or not the staphylococcus was accompanied by other organisms, in this series of cases the resulting lesions had constant, distinctive and easily recognized characters, quite unlike those of other forms of pneumonia. It is clear that it was the staphylococcal infection which determined the characteristic form of the lesion. It may therefore be claimed that staphylococcal pneumonia (whether 'primary' or not in the sense that the staphylococcus is the first or only bacterial invader) is a definite pathological entity.

Summary.

Ten cases of staphylococcal pneumonia in children are described. Four cases represent the earlier stages, with serous pleural effusion; six the later stage, with empyema.

The children's ages ranged from sixteen days to three-and-a-half years, but eight were under one year.

In nine cases staphylococcus aureus was isolated; in one case staphylococcus albus.

In six cases, as far as bacteriological investigation showed, staphylococcus was the only infecting micro-organism. In four cases there was a mixed infection.

At the earlier stages staphylococcal pneumonia is characterized by massive consolidation of one or more localized areas of one or both lungs, without generalized bronchitis. Haemorrhage and early onset of suppuration are constant features. Suppuration especially attacks the bronchi and lymph vessels.

At the later stage the affected part breaks down into a group of ramifying abscess cavities, one or more of which may burst through the pleura. This gives rise to empyema or pyo-pneumothorax.

The pathological anatomy indicates that infection reaches the lungs via the bronchi. Aspiration of food is a possible cause in some cases, especially in weakly infants.

Staphylococcal pneumonia is an entity presenting distinctive pathological characters.

Thanks are due to Professor Charles McNeil, Dr. Lewis Thatcher and Dr. J. McNair Murray for permission to publish these cases, and for the use of the clinical records of patients in their wards.

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ECTOPIA CORDIS CUM STERNI FISSURA

BY

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Examples of ectopia cordis are relatively rare, but so striking that they have long been recognized and described, and so have accumulated. In 1818 these cases were classified by Weese¹ into three main groups; ectopia cordis cum sterni fissura, ectopia supra-thoracica and ectopia sub-thoracica, and in summaries this classification has in the main been adhered to. Despite this, cases recorded are as a rule simply termed examples of ectopia cordis, and confusion has been increased by this term in several instances having been so extended as to include cases of dextero-cardia. This paper is concerned with a small group of cases in which, in association with a divided sternum, the heart lies completely outside the body, 'As if,' writes Ignatius de Torres,² 'the heart, not bearing so close a confinement, burst through the breast, and, having broke the sternum, appeared on the outside.' The case to which Torres refers is the one that was most graphically described by Martinez³ in 1723. Subsequent cases have been described by Walter⁴, Tourtelle⁵, Cruveilhier and Monod⁶, Jones⁷, Daniell⁸, Schlesinger⁹, Barnardo¹⁰, Lilwall-Cormac¹¹, Matteucci¹², Ellis¹³, Greiffenberg¹⁴, Rolland¹⁵, Cosgrove and St. George¹⁶, Cutler and Wilens¹⁷, Bloch¹⁸, Siemens¹⁹, Ledényi²⁰.

Case report.

The patient here reported represents the nineteenth in this short series (fig. 1).

R.S. was admitted into the Royal Victoria Infirmary, Newcastle, under the care of Dr. George Hall, on 9.9.35. He was barely a day old, born of healthy parents, the delivery being normal, and pregnancy uneventful. He was the second child and his elder brother was normal, as were also his cousins. He died on the evening of the next day, having been in hospital forty-eight hours. As shown by the photographs, he was well nourished and in excellent general condition apart from a gross hare lip and the pulsating tumour which lay in the midline of his chest. This consisted of the heart which was completely outside the thorax, was foetal in type, and lay vertical to the thoracic wall, the right ventricle facing the chin and the left the toes; at the base of the heart lay the two auricles, the left auricular appendage to the left and the right to right, the vessels of the heart forming the pedicle. With each respiration the heart was pulled into a more vertical position and drawn in, as was clearly demonstrated by a plethysmograph tracing.

As was previously noted by Martinez, handling the heart appeared to distress the child, but when left alone he appeared to be perfectly contented, took nourishment readily from a spoon, and was only very slightly cyanosed. In view of the previous failures reported, no attempt

at radical cure was made, and the child was made as comfortable as possible, the heart being enveloped in gauze soaked with warm saline.

Post-mortem examination ascribed his death to adhesive pericarditis, and Prof. Bramble Green kindly supplied the following anatomical report on the child :—



FIG. 1.

Examination of the intact specimen showed that the heart, which was forming a marked projection in the middle line of the anterior wall of the thorax, was uncovered by fibrous pericardium, and that the skin was directly continuous with the surface of the heart or epicardium. The skin edge at the line of continuity with epicardium or visceral serous pericardium was raised into a prominent collar-like ridge. The specimen was dissected by removal of the soft parts from the surface of the chest wall and cleaning the great vessels entering and leaving the heart.

THE HEART (fig. 2). This consisted of a large ventricular part continuous above with the aorta and pulmonary artery, and small atrial portions projecting on each side of the ventricular part. There was a slight groove on the ventricular part which indicated its separation into right and left cavities. Subsequent examination of the interior



FIG. 2.

confirmed the view that the right ventricle was placed anteriorly and above and the left posteriorly and below. The right atrium was larger than the left atrium, and the left horn of the sinus venosus was persistent.

INTERIOR OF THE HEART. The interior of the right atrium showed a normal atrio-ventricular foramen, and normal pectinate muscles.

A well-marked vertical ridge, starting above and passing down behind the orifice of the superior vena cava, seemed to separate the atrium proper from the sinus venarum or right part of the sinus venosus. There was within the latter cavity the orifice of the inferior vena cava with its valve, a small but patent foramen ovale, and below this a large opening leading into the left horn of the sinus venosus.

The interior of the left atrium presented no unusual features.

The interior of the right ventricle presented a U-shaped cavity, the descending limb passing downwards and to the left from the atrio-ventricular orifice and the ascending limb passing upwards to the orifice of the pulmonary artery. The lower muscular part of the interventricular septum was complete and ended above in a concave upper border. Above this there was a communication with the upper part of the left ventricle where the aortic orifice was plainly seen. Examination of the interior of the left atrium and left ventricle confirmed the deficiencies of the septa noted above.

THE GREAT VESSELS. The aorta appeared to be normal in its arrangement and in the arrangement of the branches which arose from it, innominate, left common carotid and left subclavian.

The veins entering the heart from above were the right and left superior venae cavae. The right vena cava was definitely larger than the left and opened into the posterior part of the right atrium. It received the azygos vein. The left vena cava opened into the left horn of the sinus venosus and also received a vein of the azygos system. The two venae cavae were joined just below the thyroid gland by the transverse communication which normally should form the left innominate vein. Two large inferior thyroid veins joined this vessel.

The pulmonary artery appeared to be normal as to its division, but there was no communication (ductus arteriosus) with the arch of the aorta. The other vessels, as far as could be seen, also seemed to be normal.

The condition of the skeleton of the anterior chest wall was interesting. There were two sternal bars widely separated above, each of which was joined to the first seven costal cartilages and articulated above with the clavicle. The lower ends of these sternal bars were joined by a cross-piece which formed an interior boundary to the aperture through which the heart protruded.

SUMMARY.

The main anatomical features of the specimen were :—

- (1) Complete extrusion of the heart from the thorax.
- (2) Absence of the parietal pericardium.
- (3) Incomplete development of the ventricular and atrial septa.
- (4) Persistence of the left horn of the sinus venosus.
- (5) Absence of the ductus arteriosus.
- (6) Developmental arrest of sternum.

Discussion.

It is significant that the description by Martinez had almost applied to this child or to the majority of children in this series, for, with the exception of the child reported by Matteucci, whose heart was apparently covered by skin and a normal pericardium, and those by Cosgrove and Ledényi, who had died some time before birth, and in whom there

were other gross abnormalities, these cases all have a great deal in common.

As a rule pregnancy was uneventful, though in several instances^{15, 10, 5, 7}, the child was born prematurely. Moreover, only once¹⁵ did the child die in the course of delivery, owing, it was thought, to pressure on the exposed heart, and this child was born prematurely at six-and-a-half months, and, it so happened, one of twins, the other twin, a dissimilar one, being normal. Boys are more commonly affected than girls, for ten of this series were recorded as being male and only six female, and it seems probable that all races of man are equally affected. This abnormality is not infrequently met with in animals. Though one child recently lived for as long as eight days¹⁸, as a rule such children live for a bare one or two days, the average duration of life being thirty-six hours. Recently there has been an attempt in two cases^{17, 18} to prolong their life by restoring the heart to the chest cavity and covering it over with skin-flaps. In both instances the action of the heart immediately became so embarrassed as a result of external pressure that it was necessary to cut the sutures and release the heart. The most successful treatment at present, then, would still appear to be with a few modifications, that introduced by Martinez, who had made in imitation of the pericardium a little chest of pliant osiers and around this draped a small linen cloth soaked in spirits of wine and melted butter.

Permission for an autopsy in the first-reported case was obtained only after repeated entreaties. In some of the subsequent cases complete examinations were not carried out. With the exception of the case already mentioned, reported by Matteucci, the pericardial sac appears invariably to have been lacking in these children, the parietal pericardium alone covering the heart, and in the majority of instances forming a prominent line of junction with the skin. Frequently^{4, 8, 9, 10, 14} the foramen ovale was patent, and in these cases, with one exception¹⁰, the inter-ventricular septum was also incomplete, while the presence of two superior venae cavae was noticed in several cases^{4, 9, 14, 16} in addition to the one here reported. As a rule the fine general condition of the child has been stressed, but the hare lip and cleft palate, which was so prominent a feature in this child, are also present in some degree or other in several of the series^{4, 11, 12, 16, 19}, and were present to a gross extent in the two babies^{16, 20} previously noted, who were born dead.

Electrocardiograms.

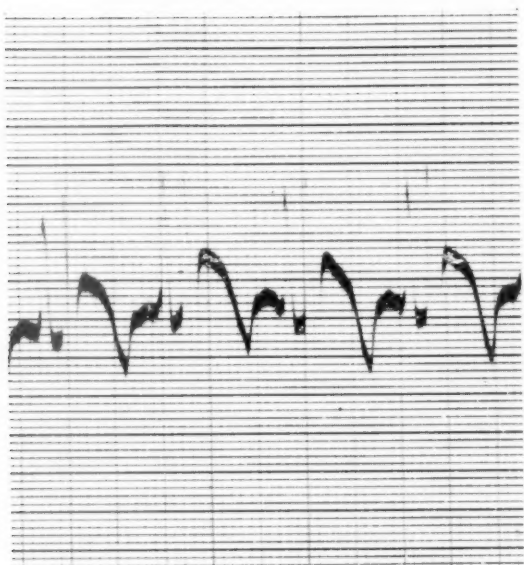
In only one patient, prior to that reported here, have electrocardiograms been taken, and Bloch¹⁸ contents himself with stating that they revealed a normal pulse rate of 130-140 beats per minute. It was felt, therefore, that in this child an attempt should be made to confirm the recent work by Barker, McLeod, and Alexander²¹ on direct stimulation of the heart muscle. As might have been anticipated, since the

heart lay right outside the child's body, electrocardiograms taken from the ordinary leads revealed very little indeed, the heart itself causing scarcely any deflexion at all. Use was therefore made of non-polarizable electrodes and a series of tracings made from direct leads taken from the heart. Such curves have been termed by Samojloff²² electrograms in order to distinguish them from the electrocardiograms taken from indirect leads. In any consideration of these it is important to bear in mind their fundamental differences from the electrocardiogram, for, whereas by virtue of their broad contacts, which are constituted by the tissues surrounding the heart on all sides, the electrocardiographic curves represent much more in their due proportions the activity-effects of all the muscle of the chambers, the electrogram represents simply the result of differences in potential in relatively small areas of muscle lying immediately in contact with the two electrodes. Many of the characteristics of the electrocardiogram appear to depend upon the nature of the contacts rather than upon the heart itself, so that, as shown by Kountz, Prinzmetal and Koenig²³, the dog's heart suitably placed in the human pericardial cavity may yield with the normal leads electrocardiograms 'similar to those obtained with the revived beating human heart.' Though, then, another paper²¹ of theirs suggests that electrocardiograms taken from the human heart may not in the future be so rare as at first sight one might expect, it would seem reasonable to believe that a great deal of the experimental work done by Craib²⁵, Samojloff²², Woronzow²⁶, Lewis²⁷ and his co-workers in the animal is applicable to the interpretation of electrograms in man, and more particularly to those of this child.

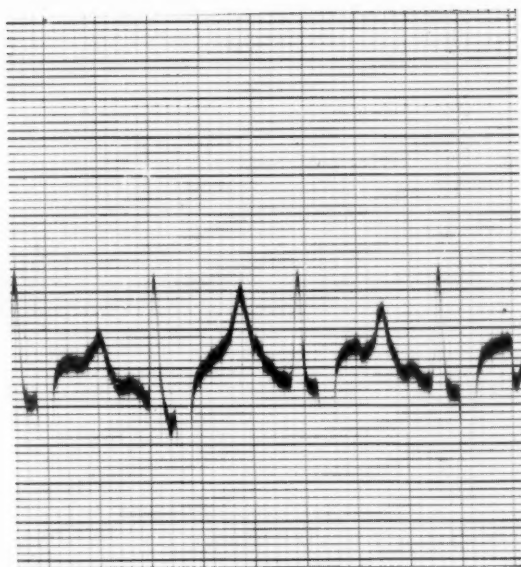
The electrograms in this case were taken as follows:—

As is more clearly shown in fig. 2, a definite sulcus separated the apices of the two ventricles. Three different leads were therefore employed, the first being from the right apex and the left base, the second from the left apex and the right base, and the third from the lateral extremities of the right and left auricles. Non-polarizable electrodes were used. They were of the form described by Gotch²⁰ and employed by Lewis²⁷, with the exception that contact with the surface of the heart was made by means of camel-hair brushes dipped in the kaolin-saline paste and protruding through the end of the glass tube. Electrograms (fig. 3) taken from these leads are here designated a, b and c. The electrograms c and d were taken from the same leads as a and b respectively, but differ in that prior to their taking cold was applied to the tip of the left ventricle in the first electrogram and to the right in the second. This was in both instances effected by means of a test-tube filled with cold water and applied for 30 seconds before the electrogram was made. The sixth (f) tracing represents a normal electrocardiogram (Lead II) taken from this child, and the seventh (g) an electrocardiogram taken with one lead on the left ventricle of the child and the other on the lower skin of the lower part of the abdomen.

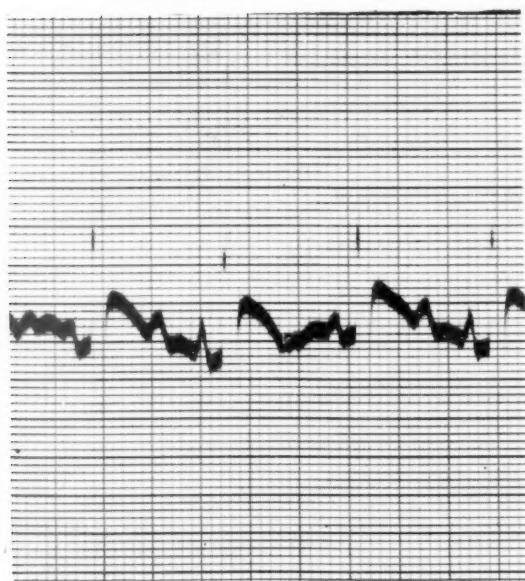
It is apparent that these curves differ from those obtained from the ordinary leads, and their interpretation is rendered peculiarly difficult in that it was impossible in this case to take normal electrocardiograms



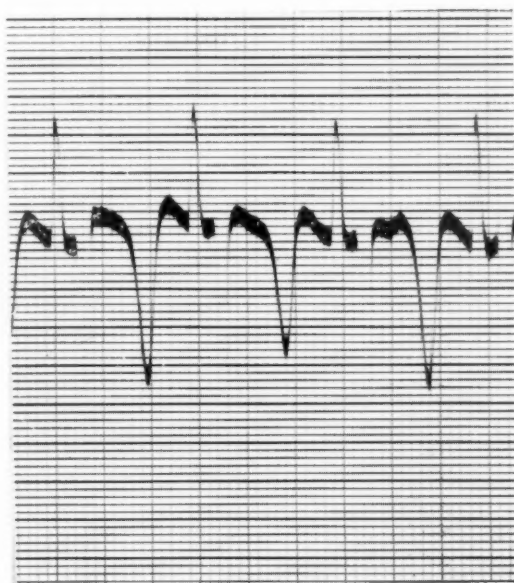
A



B



C



D

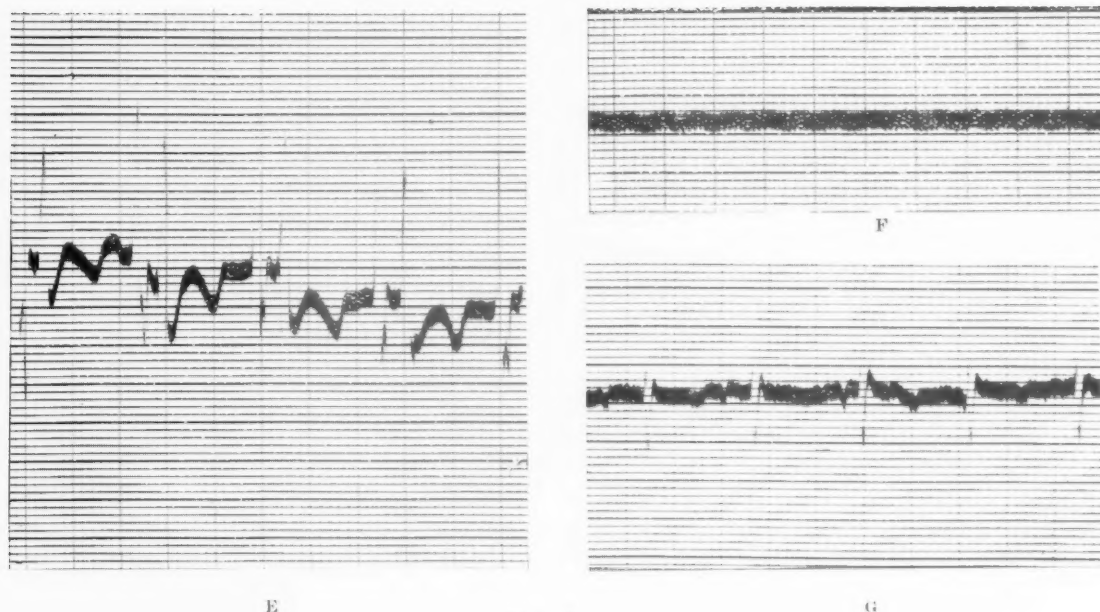


FIG. 3.

to act as a control. Moreover, the area of the electrodes in contact with the heart is relatively large compared to, for instance, those employed by Lewis who used electrodes having a contact area of 1.5-2 mm. in diameter, whereas the diameter of the ones we employed were from two to three times greater. Furthermore, these electrodes were placed at a considerable distance from one another. Now, as Craib²⁵ has shown, in such circumstances a peculiarly complicated curve may be expected, for such a curve represents not merely the resultant of changes in potential due to processes which have reached the two electrodes at approximately the same time, but rather a resultant due to processes which will have been initiated at different times in the two electrodes.

A further difficulty inherent in all considerations of electrograms lies in the fact that, as Lewis²⁸ points out, curves from electrodes applied directly to cardiac muscle comprise deflexions of two kinds.

'The chief deflexions are those which result from the arrival of the excitation process immediately beneath the contacts; these are termed intrinsic. They are deflexions, which represent relatively large electrical potentials, and they have correspondingly large amplitudes. (Exceptionally the intrinsic deflection is not the most prominent in the electrogram.) The deflexions of the second order are those yielded by the excitation wave travelling in distant areas of muscle. These are qualified by the adjective extrinsic.'

Thus it is apparent as Lewis²⁹ remarks elsewhere, 'that we cannot be too circumspect in interpreting curves taken by leads direct from the heart muscle.'

Ultimate understanding of them would seem in the main to depend upon observing the effects of experimental change in the conditions under which such electrograms are taken, and it is only too apparent that the simple and somewhat clumsy experiment here reported would in normal circumstances represent one of a prolonged series of carefully controlled and repeated experiments. It will be noted that the application of cold to the surface to the right and left ventricles produced, as shown in c and d (fig. 3) very considerable changes in the deflexions of the electrograms taken from those leads, but the significance of these changes and their interpretation would appear to depend upon the carrying out of further experimental work.

Summary.

A case of ectopia cordis has been described. Electrocardiograms and electrograms were taken and the effects of cold on the electrograms recorded. It is felt that the interpretation of these results is dependent upon a further experimental investigation, but by virtue of the rarity of the conditions under which they were taken they appear to merit recording.

It is a pleasure to have this opportunity of thanking Dr. Hall for permission to publish details of this case admitted to his care, Professor Hume for the interest he has taken in it, and Dr. Carr for the assistance he gave in the taking of the electrograms.

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THE CARBOHYDRATE METABOLISM IN ABDOMINAL TUBERCULOSIS

BY

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It has long been taught by eminent clinicians, notably the late John Thomson, that cases of abdominal tuberculosis, especially where there is much diarrhoea, or loss of weight, do best on a diet containing a liberal allowance of protein with some restriction of carbohydrate. It was in the hope of throwing some light on this more or less empirical fact that the work to be described was undertaken.

At the outset, the obvious suggestion was that there might be a defective power to absorb carbohydrate from the bowel, just as in some of these cases there may be a relative inability to absorb fat. Such a defect is not so readily demonstrable as a steatorrhoea, the examination of the faeces for carbohydrate residue being an unsatisfactory procedure. One suggestive fact was already available, namely that the oral glucose tolerance curve may be flat in these cases. It was decided to try to ascertain the significance of this curve by carrying out intravenous glucose tolerance tests as well.

The test employed consists in the injection into a vein of the fasting patient of 10 gm. of pure dextrose as a 20 per cent. solution in normal saline, the time taken for the injection being from one to three minutes according to circumstances. Specimens of blood are taken from a prick in the warmed lobe of the ear at intervals of two minutes at first, and later of five or ten minutes, the whole observation extending over an hour.

Results and discussion.

Three cases were examined in this way. In all three, oral curves of a fairly flat type were found (fig. 1), the fasting level in two of the patients being notably low (64 and 66 mgm. per cent. respectively). The rises from the fasting level to the peaks of the curves were 72, 29 and 68 mgm. per cent., figures of which one only is strikingly low, and which might escape comment. The intravenous curves, however, were all of a high type (fig. 2) indicating gross impairment of tolerance.

There was thus presented the seeming anomaly of oral curves tending to be flat with intravenous curves of the opposite form, and there appears to be only one ready explanation of this, namely an absorptive defect. If such a defect exists, then the low oral is obviously explained. Further, according to present beliefs the glucose tolerance of a healthy individual is determined solely by the amount of carbohydrate the diet has contained for the period preceding the test. An absorptive defect should produce the

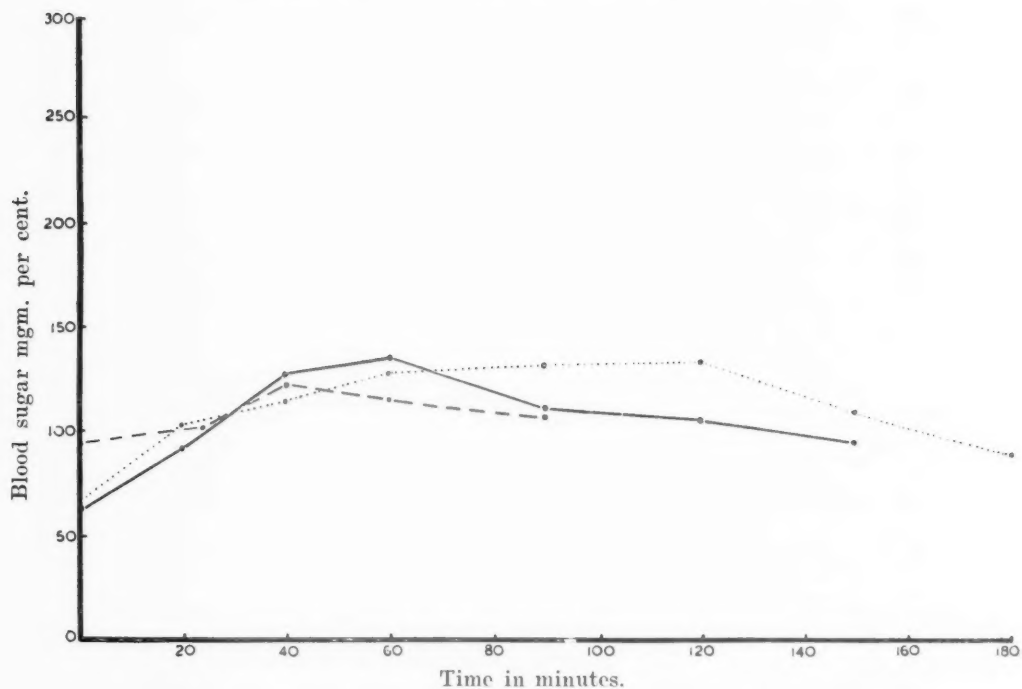


FIG. 1.—Flat blood sugar curves obtained after giving 30 gm. of glucose orally to each of three cases of abdominal glandular tuberculosis.

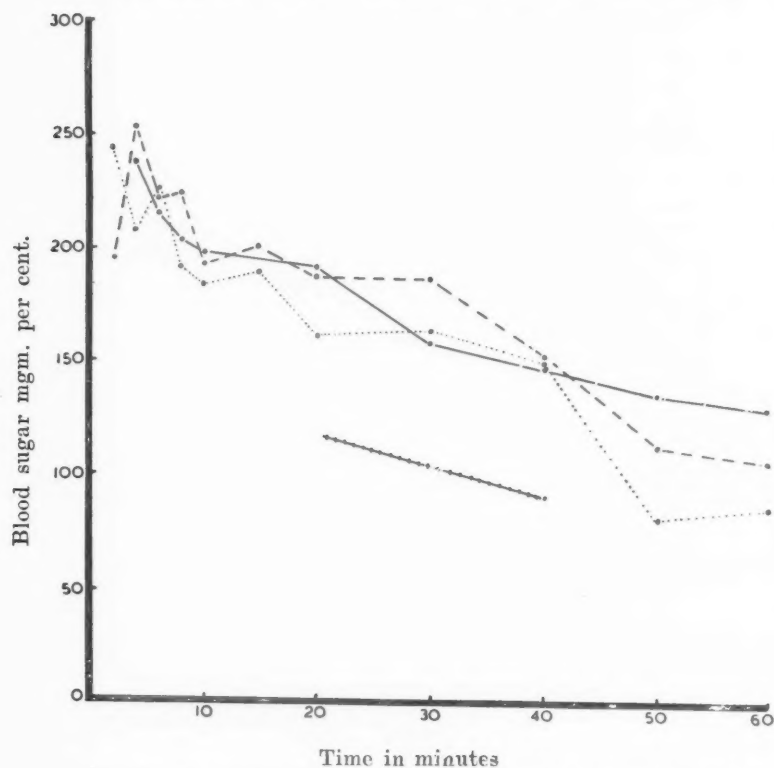


FIG. 2.—High intravenous blood sugar curves obtained from the same three cases as the oral curves in fig. 1. A small section of a normal curve is included for comparison.

same effect as carbohydrate deprivation in this regard, and hence the intravenous curve should be high. The anomaly is explained on this basis.

A further point of rather a confusing nature should be cleared up at this stage. As mentioned earlier, the rise from fasting level to peak following an oral test dose of sugar was not strikingly small in two of the cases examined, and this might be thought at once to rule out any absorptive defect. Actually, however, the curves obtained in a case of moderate absorptive deficiency must reflect the resultant of two opposing factors. On the one hand, the fact that only a small part of the sugar given actually reaches the blood might be expected to give a low curve. On the other, if the patient is otherwise healthy the deprivation of carbohydrate must be expected to lead to impaired tolerance and a high curve, there being an abnormal rise in blood sugar level in response to each moiety of sugar actually reaching the blood. It is the interaction, it is suggested, of these two opposing factors which may lead to a curve in some respects approaching normal.

It may be raised as a criticism that diarrhoea alone might amount to a sufficient absorptive defect. Opportunity arose to re-examine one of these cases during a period of severe diarrhoea and again during a remission and the curves show little, if any, significant difference.

All of these cases were of the glandular type with easily palpable abdominal glandular masses, and in two of the cases calcification of some of the glands was revealed by x-ray. Opportunity recently offered to study similarly an ascitic case, in which no gross glandular involvement was discovered, and there had been no diarrhoea, though wasting was gross. The result here was an interesting contrast, the curves (fig. 3 and 4) being in all regards comparable to those of a normal patient on a very low carbohydrate diet, i.e. both oral and intravenous curves were high, and it is inferred that there was little or no absorptive defect. What then, was the cause of the impaired tolerance? In this respect it is dangerous ground to suggest that the causal agent was the tuberculous toxæmia. Evidence that this was present included a fairly high temperature and rapid pulse rate. It may be mentioned that the same tests have been carried out on two other tuberculous patients—one suffering from coxalgia, the other from a large retroperitoneal mass of tuberculous glands. The former was clinically ill and toxic-looking and showed similar curves of much milder degree. The latter was clinically well and gave a perfectly normal intravenous curve.

Treatment.

The bearing of these observations upon treatment was next considered. According to current ideas, degrees of glucose tolerance or intolerance are caused by the presence in circulation of more or less 'insulin-kinase,' a third factor in the insulin-glucose reaction which is probably prepared for the

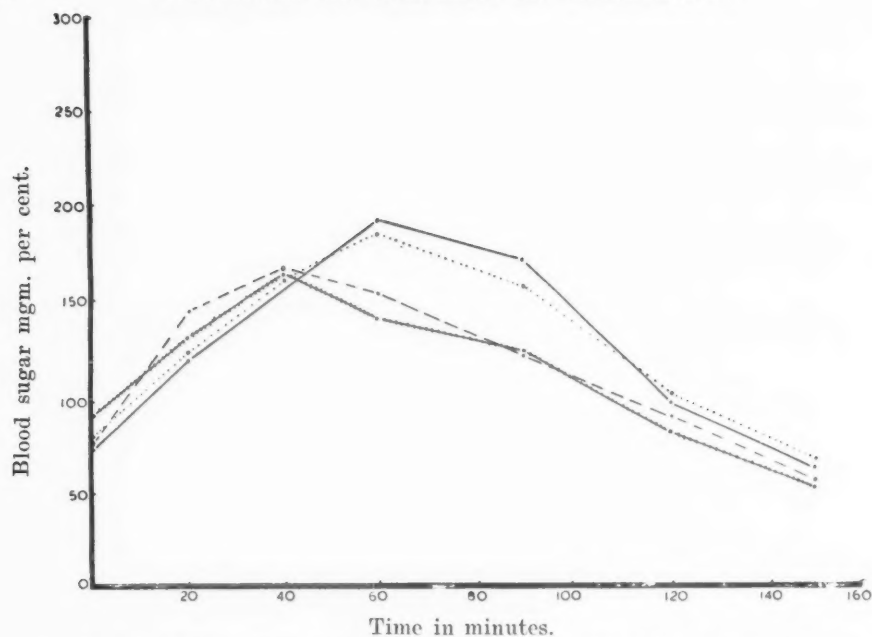


FIG. 3.—Oral curves from an ascitic patient. The solid line represents the original condition; the dashed line the effect of giving 2 c.c. of Campolon intravenously prior to the test; the dotted line the condition after withholding liver treatment for eleven days; the crosshatched line the effect of giving one-half ounce of liquid extract of liver by mouth twice a day for eleven days.

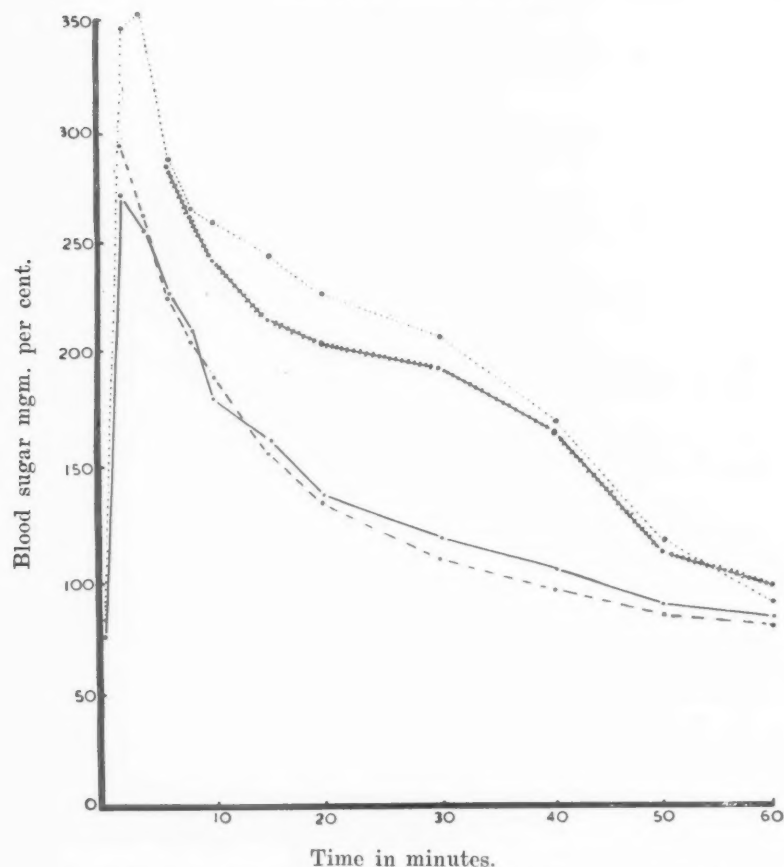


FIG. 4.—Intravenous curves obtained from the same patient as the curves in fig. 3 under the same conditions. The dotted line represents the original condition; the dashed line the effect of Campolon; the cross-hatched one the reversion on withholding liver treatment; the solid one the effect of liver treatment by mouth.

greater part in the liver. Previous work had led to the belief that this substance was present in 'Campolon.' Accordingly, the worst of the three glandular cases was given 2 c.c. of 'Campolon' intravenously six minutes before a further intravenous tolerance test. The resulting curve (fig. 5) was strikingly altered towards normal, and in fact was for practical purposes normal. The patient was then left untreated for four days and again tested without 'Campolon.' The curve had reverted to its previous level. He was then given one ounce of liquid extract of liver orally daily, and curves

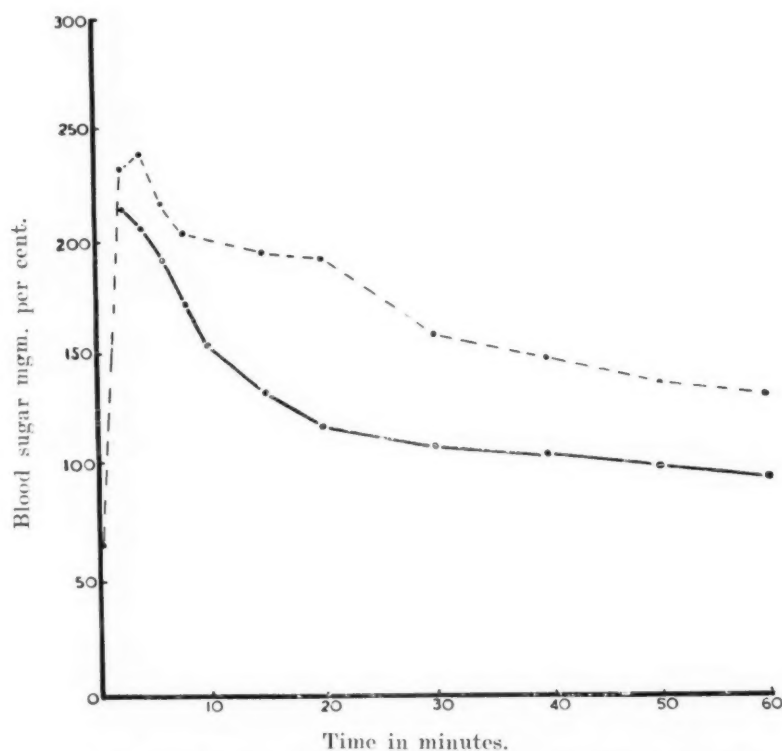


FIG. 5.—Curves obtained from a severe glandular case. The upper one represents the state before treatment with Campolon, and again after cessation of liver treatment for four days; the lower one was obtained after intravenous Campolon and again after two weeks and after twelve weeks on liver extract by mouth.

obtained in two weeks and in twelve weeks, practically overlies that obtained with 'Campolon.' An almost identical series of tests was carried out on the ascitic case, and showed a corresponding improvement of tolerance, both intravenously and orally (fig. 3 and 4).

As to clinical results, the treatment proved most striking. Both patients had the advantage of rest in bed and of diets which were adequate even if the carbohydrate were disregarded. The patient with glandular enlargement was admitted to hospital with the gravest possible prognosis from a convalescent home of which he was no longer a proper inmate. He

had been bedridden for months up to the commencement of treatment and was shockingly wasted. In three months' treatment he gained $11\frac{1}{2}$ lbs. in weight and improved to the point of being up and actively running about. The patient with ascites who was also given an early fatal prognosis on admission, has lost all her ascites, gained eleven pounds notwithstanding, and, while still in bed, feels and looks perfectly well. In neither patient was there any blood disorder more grave than a mild anaemia of secondary type which improved slightly under treatment. There is no evidence that the absorptive defect in the glandular type of case is materially improved by liver treatment.

Permission to report the cases referred to was granted by Professors L. G. Parsons and K. D. Wilkinson and Dr. J. M. Smellie. All the blood sugar determinations involved in this work were carried out by Miss Eva Tonks, Assistant Biochemist to the Hospital, to whom thanks are due.

MORQUIO'S DISEASE

REPORT OF TWO CASES

BY

PEARL SUMMERFELDT, M.B.,

AND

ALAN BROWN, M.D., F.R.C.P.(C)*.

In 1929 Morquio¹ described an osseous condition characterized by a widespread, symmetrical deformity of the skeletal system. It was characterized by a shortening of height and an anterior posterior deepening of the thorax. In contrast, the extremities have normal dimensions, although there are deformities present such as flat feet and genu valgum. Since then, Ruggles², Meyer and Brennemann³, Barnett⁴, Davis and Currie⁵, and Coward and Nemir⁶, have published reports of similar cases. In all there have been eighteen cases reported. The familial occurrence of the disease is most marked, there being only three cases on record where only one member of a family was affected.

Case records.

Two brothers were admitted at different times to the hospital. The younger (S. S., aged 9 years) was admitted in October, 1934, while A. S., aged 11 years, was admitted in April, 1935. The parents who are not related are alive and well. There are also two sisters and two other brothers who are all normal. No information could be obtained of the presence of this deformity in the preceding generation. The children had always lived on a farm and had never received any cod-liver oil in infancy or early childhood. Both children were admitted with a complaint of deformity of the back from early childhood. In addition, during the past two years the gait of the younger brother had become waddling in character.

The physical appearance of both children was similar, though in the younger brother the changes in the osseous system were more marked (fig. 1 and 2).

HEADS: These appeared to be larger than normal and square in shape. The bridge of the nose was depressed. The facial expression was bright and alert. The teeth were malformed in the older patient.

TRUNK: The trunk appeared to be short due to changes in the vertebral bodies (see fig. 3). There was a marked kyphosis in the upper lumbar region. The sternum projected forward in the

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upper three-quarters and curved in below this. There was some flaring of the costal margins and the anterior posterior diameter of the chest was greater than the transverse diameter. The costal margin nearly rested on the crest of the ilium.

EXTREMITIES: There was a wide-base gait which in the younger brother resembled that of dislocation of the hip. In the standing position a marked genu valgum resulted in a separation of the



FIG. 1.—Photograph of S. S.,
aged 9 years.

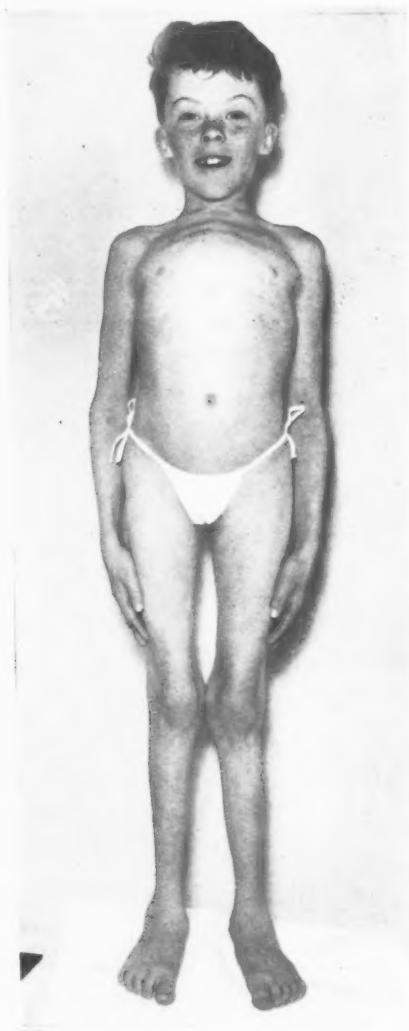


FIG. 2.—Photograph of A. S.,
aged 11 years.

feet of four inches. The feet were very flat. The bones of the extremities were fairly straight. The finger tips nearly reached the level of the knee.

MUSCULAR DEVELOPMENT was fairly good but in the younger brother it was better on the right side than on the left. There was some muscular weakness but no limitation of movement.

The liver and spleen were not palpable. The eyes were normal.



FIG. 3.—X-ray of vertebrae (A. S.)—lateral view, showing deformity of vertebral bodies.

TABLE I.
PHYSICAL MEASUREMENTS.

	9 YEARS NORMAL (ENGLEBACK) 1932	9 YEARS S. S.	11 YEARS NORMAL (ENGLEBACK) 1932	11 YEARS A. S.	7 YEARS NORMAL (HOLT)	7 YEARS MEYER & BRENNEMANN
HEAD	20.9 inches	23 inches	21.1 inches	21½ inches	20½ inches	21 inches
CHEST	24.6 "	24 "	26.1 "	27 "	24 "	37½ "
ABDOMEN	22.3 "	22 "
TOTAL LENGTH	51 "	46 "	55 "	51 "	36 "	32 "
WEIGHT	57 lb.	50½ lb.	70 lb.	51 lb.	56 lb.	31 lb.
SITTING HEIGHT	26 inches	23 inches	23 inches	19½ inches

TABLE 2
CLINICAL AND LABORATORY INVESTIGATIONS

	S. S. 9 YEARS	A. S. 11 YEARS
URINE ANALYSIS	Normal	Normal
CONCENTRATION TEST	Normal limits	Normal limits
TUBERCULIN SKIN TEST 1/400 DILUTION	Negative	Negative
BLOOD WASSERMANN	Negative	Negative
INTELLIGENCE QUOTIENT	124	—
B. M. R.	99 per cent. (B. & T.)	100 per cent. (B. & T.)
BLOOD PRESSURE	108/82	120/90
CALCIUM MGM. PER 100 C.C. BLOOD ..	9.1—9.9	10.3—9.9
PHOSPHOROUS MGM. PER 100 C.C. BLOOD	4.9—5.0	4.4
PHOSPHATASE	12.6 units	19.2 units
N. P. N.	43 mgm.	36 mgm.
CREATININE	1.66 mgm.	1.25 mgm.
CALCIUM RETENTION FOR 4 DAY PERIOD RECEIVING AN INTAKE OF 1 GM. OF CALCIUM DAILY	+ 2.95 mgm.	+ 2.387 mgm.
CALCIUM RETENTION FOR 3 DAY PERIOD RECEIVING AN INTAKE OF 100 MGM. OF CALCIUM DAILY	- .378 mgm.	- .336 mgm.

In table 1 are seen the measurements of both boys and also the measurements of the case reported by Meyer and Brennemann³. It will be noted that the three children are three to four inches shorter than the normal total height. This shortening is chiefly due to changes in the vertebral column,

as the sitting height is less than normal for that age. The greater chest measurement of the case reported by Meyer and Brennemann is possibly due to the fact that the kyphosis was in the thoracic region, while in the two patients here described it occurred in the lumbar areas. All children were under weight.



FIG. 4.—X-ray showing changes in knees (S. S.).

In table 2 are seen the results of the clinical and laboratory investigations. The findings were all within normal limits. It is of interest to note that on an intake of 1 gm. of calcium per day there was a positive balance, while on an intake of 0.1 gm. of calcium per day there was a

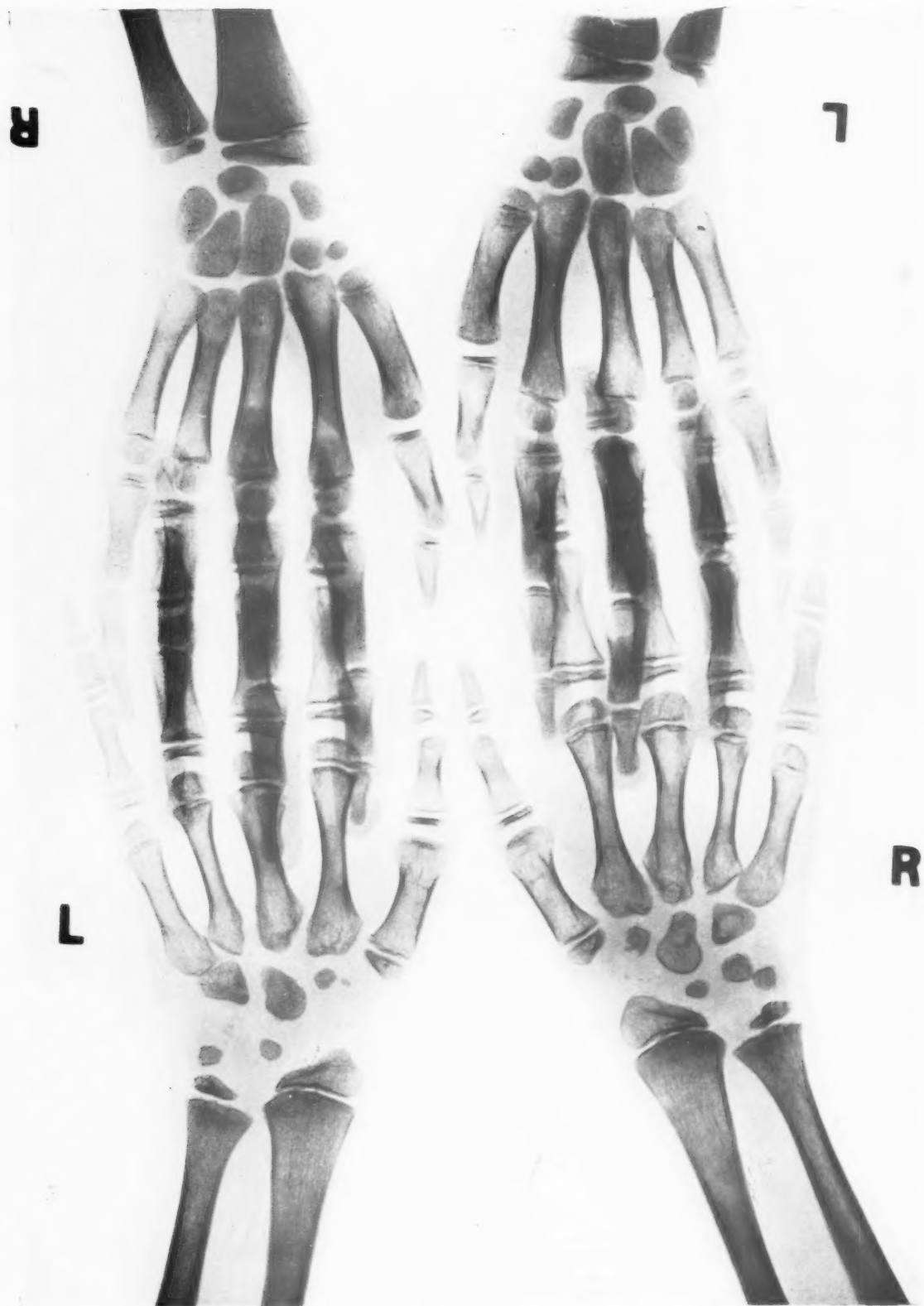


FIG. 5.—X-ray of hands of A. S. and hands of normal child same age. This shows decreased number of centres of ossification and osteoporosis. There is malformation of proximal ends of metacarpal bones.

negative balance. A normal boy, ten and a half years of age, who was placed on similar diet containing 0.1 gm. of calcium per day at the same time also showed a negative calcium retention.



FIG. 6.—X-ray of pelvis and upper ends of femur (A. S.), showing changes in contour of pelvis and heads of femora.

X-ray findings.

Dr. A. Rolph, radiologist to the Hospital for Sick Children, Toronto, has made the following report of the skiagrams that were taken of the entire skeleton. The bony changes were similar in each case.

All the vertebrae show a considerable degree of osteoporosis combined with a curious change in shape. For the most part they are under-developed. In all cases the vertical diameter of the bodies is diminished and a considerable degree of lordosis has been produced in the lumbar region. The first and second lumbar vertebrae are short in the anterior posterior diameter (fig. 3).

Skiagrams of the long bones show a considerable degree of general osteoporosis and the epiphyses are very irregularly formed. At the elbows it is noted that the epiphyses on the medial and lateral aspects are

so developed as to make the lower end of the humerus almost symmetrical. The trochlea is distinctly under-developed. The medial epicondyle is abnormally developed, being an irregular mass of small centres of ossification which spread out in semilunar formation. At the wrists there is a distinctive under-development of centres of ossification. At the knees (fig. 4) the epiphyses of the femora and tibia are very irregular in outline, appearing almost angular at points along their articular surfaces.

Skiagrams of hands (fig. 5): The ends of the third and fourth metacarpals are deformed, some having a pointed base instead of the usual flat ends. These findings correspond to the skiagrams in the case reported by Meyer and Brennemann.

Skiagrams of the hips (fig. 6): The pelvis is distinctly deformed, having a pinched-in appearance from side to side. The acetabular cavities are unusually enlarged, and their articular surfaces are irregular. The heads of the femora show flattened epiphyses which are very poorly developed and mottled, and somewhat like those bones in Legg-Perthe's Disease. Both sides have the same changes.

Skull: This shows an unusually high cranium, with unusually thick bones forming the cranial vault. They have a slightly more granular appearance than normal. The sella turcica appears small.

Intravenous pyelograms of the urinary tract were normal in each boy.

Comment.

Clinically the outstanding findings are dwarfism and deformity of the body due to changes occurring chiefly in the vertebrae, pelvis and long bones. There is delayed epiphyseal development and retardation of the centres of ossification. At present this condition might be confused with a somewhat similar osseous condition described by Poynton⁷ and others in which dwarfism is associated with bony changes in the skull as well as the skeleton, splenomegalia, enlarged liver, and defective vision.

From the x-ray examination it would appear that some process was interfering with normal development of the epiphyses, the centres of ossification.

No explanation is offered for the etiology of this condition. It has already been suggested by others that the condition might be related either to a metabolic or endocrine disturbance. Ruggles has treated his cases with both pituitary and thyroid extract. The results were disappointing. Meyer and Brennemann gave their cases 90 drops of viosterol a day for five months, which caused a rise in phosphorus and a drop in the calcium values, but there was no improvement in the osseous system. The younger of the present patients was given three tablespoonsful of cod-liver oil daily and Mead's Mineral Mixture No. 5, receiving 1 tablet thrice a day. He did not take the cod-liver oil but did take the calcium tablets. The mother reports a gain in height but as yet he has not been admitted for a re-examination. The older brother was put on thyroid, $\frac{1}{2}$ grain daily.

Summary.

A report is presented of two brothers with a generalized, symmetrical osseous disturbance resulting in dwarfism and peculiarly shaped chest. Radiologically the chief changes appear in the vertebrae, pelvis, long bones, and delay in the development of the epiphyses especially of the head of the femur. The condition has a tendency to be familial and its etiology is unknown at present.

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NOTICE TO CONTRIBUTORS

It is proposed to publish from time to time reports of single cases which are of special interest and importance.

CASE REPORT

SUBCUTANEOUS RHEUMATIC NODULES WITH NO CARDITIS

BY

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(From the Department of Medicine, University of Bristol, and the Bristol General Hospital.)

The following case of acute rheumatism in a child with an abundant crop of subcutaneous nodules as the most outstanding feature is unusual in the absence of any evidence of a cardiac lesion clinically or at autopsy. The association of these nodules with other manifestations of acute rheumatism is widely recognized, and was described fully by Cheadle in 1889. Subcutaneous nodules, however, almost invariably occur with carditis, and generally appear late in the course of the disease. In this case the nodules, apart from vague joint pains, were the only definite sign of the rheumatic infection, and at the time of death, seven weeks after their first appearance, there was no evidence at all of cardiac involvement.

HISTORY. The patient, a boy of eleven, was first seen in October, 1935, by Prof. C. B. Perry. For the last month his fingers, wrists, shoulders, back, and knees had been stiff, and he could not run or stoop, but could ride a bicycle. Previously he had had measles, whooping cough, chicken-pox, erysipelas, and bronchitis, and an illness in February, 1935, which was diagnosed as glandular fever.

PHYSICAL EXAMINATION showed a thin, pale boy, but no definite physical lesion could be made out, and the joints appeared normal. He was a highly-strung, nervous child. At this time he appeared well and the history was so indefinite, that he was referred back to his doctor for observation.

FURTHER COURSE OF ILLNESS. Seen later at the end of November the joints of the fingers of both hands were swollen, and rheumatic nodules were present on both elbows. The boy was admitted to hospital on December 2. He was thin and pale. There was an extensive crop of nodules over his elbows, knees, along the extensor tendons on the back of the hands and over both ulnae. His finger joints were slightly enlarged, but they were painless and freely movable. The heart was normal, and no lesion was found elsewhere. During the first twelve days after admission, the temperature rose three times to 99° F., but was otherwise normal. The pulse-rate

ranged from 88–112 per minute. No salicylates were given. The nodules became more extensive but no other lesion developed. On December 13, the patient developed a typical attack of appendicitis, with epigastric pain moving to the right iliac fossa after he had vomited twice. The temperature rose to 100° F. and he was acutely tender in the right iliac fossa. He then told, for the first time, of a similar attack of pain in August, 1935, lasting for some hours. At operation the appendix was found to be thickened, slightly enlarged, and contained some pus. On section it showed evidence of acute inflammation and of changes resulting from the previous attack.

Convalescence was not entirely satisfactory, as there was slight pyrexia without localized signs. The fever continued and was unaffected by the exhibition of salicylates, and no cause for it could be discovered in the heart, chest, or abdomen. On January 8, 1936, an impaired percussion note was detected at the left base with absence of breath sounds. These signs increased, and on January 13 the chest was explored and 8 c.c. of clear yellow fluid were withdrawn. On culture this gave a mixed growth of *B. coli* and pneumococci. The condition of the patient became rapidly worse, with tachycardia, dyspnoea, and cyanosis, but without cough or sputum. He died on January 18. During this post-operative period the nodules gradually disappeared, and at the time of death none could be found.

POST-MORTEM EXAMINATION showed a small retro-caecal abscess containing about a drachm of pus, and two metastatic lung abscesses in the lower lobe of the left lung. The pleura was thickened and contained a little fluid. There was a slight excess of fluid in the pericardium, but the heart appeared perfectly normal macroscopically. Sections of the myocardium and mitral valve were normal, and no evidence of carditis was found.

Summary.

A case of acute rheumatism in a child is described in which there was an unusually heavy crop of subcutaneous nodules without any evidence of cardiac involvement. The patient died of intercurrent acute appendicitis complicated by metastatic lung abscesses. At autopsy the absence of a cardiac lesion was confirmed.

Prof. C. Bruce Perry, under whose care this patient was, has kindly given permission for these notes to be published.

BANTI'S SYNDROME IN CHILDHOOD :

A REPORT OF FOUR CASES

BY

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Haematemesis in childhood is a rare event which may be due to similar causes to those occurring in adults, barring malignant disease. After the age of infancy the commonest disorder in which it is found is splenic anaemia or Banti's disease. The distinction between those two conditions is ill defined; they are commonly regarded as synonymous and either diagnosis is applied to a case exhibiting splenomegaly and anaemia of obscure origin, with or without haemorrhages, hepatic cirrhosis or ascites.

Banti^{1, 2, 3} described three stages of his disease—namely a pre-ascitic stage of anaemia and splenomegaly, a short intermediate stage associated with gastro-intestinal disturbances and hepatic enlargement, and a final ascitic stage of cirrhosis of the liver with ascites. He clearly differentiated his disease from Laënnec's cirrhosis, but admitted that it resembled splenic anaemia, which he had previously described in a monograph⁴. He stated that the symptoms of splenic anaemia were identical with those of the pre-ascitic stage of his disease and that distinction was virtually impossible; but he denied that his disease merely represented the last stage of splenic anaemia—in that it occurred so rarely, and because patients with splenic anaemia of even two years' duration never developed cirrhosis of the liver.

Banti was right in this last assertion when it is realized that splenic anaemia, at that time, literally meant anaemia with splenomegaly. With the advance of medicine, those conditions in which anaemia occurs with splenomegaly but without subsequent hepatic cirrhosis—such as Gaucher's disease, Niemann-Pick's disease, acholuric jaundice and achlorhydric anaemia—have been recognized as definite entities, and are no longer classified as splenic anaemia. Nevertheless there still remains a group of cases characterized by anaemia and splenomegaly, perhaps with haemorrhage and sometimes with hepatic cirrhosis, which constitute to-day the splenic anaemia-Banti's disease group.

Banti unquestionably described a syndrome produced by various pathological processes, which may be classified as follows:—

1. VASCULAR ABNORMALITIES OF THE PORTAL SYSTEM.

(a) Thrombophlebitis of the portal or splenic veins (Warthin¹⁵) has frequently been found at autopsy, but opinion is still undecided whether they are primary or secondary features. It is doubtful if these conditions can be diagnosed during life, unless they occur in massive form, when a fatal result will inevitably ensue.

(b) Persistence of the umbilical vein has been described as a condition producing Banti's syndrome.

(c) Pressure on the splenic vein by adhesions—such as occur in old tuberculous peritonitis.

2. SPECIFIC INFECTIONS.

(a) Syphilis can produce Banti's syndrome to perfection, and responds to some extent to anti-syphilitic treatment.

(b) Malaria. Many of the cases reported by Osler^{9, 10} had a definite history of malaria—the splenomegaly of which probably disordered the portal circulation, causing Banti's syndrome.

3. NO KNOWN AETIOLOGY.

This group contains cases which Banti probably had in mind, since he emphasized the lack of etiological factors and the absence of organisms in the spleen; but he admitted occasional changes in the veins of the portal system at autopsy.

Smith and Howard¹³ and Wallgren¹⁴ described cases of haematemesis without warning in young children, in whom no spleen was palpable and secondary anaemia was the only abnormal finding. This syndrome they attributed to obstruction of the splenic vein either from thrombophlebitis within it or pressure from without. Banti's disease was differentiated by its almost constant leucopenia, because its haemorrhages were preceded by malaise and occurred later in life, and because there was no decrease in size of the spleen after haematemesis—a feature which they considered to occur characteristically in thrombophlebitis of the splenic vein.

Case reports.

Four cases showing Banti's syndrome will be described and discussed. In cases 1, 2 and 3 the Wassermann reaction was negative, and the fragility of red cells, bleeding time and coagulation time normal.

Case 1.—J. S., a girl aged 6 years, was admitted to the Middlesex Hospital on February 13, 1936, with a history of having vomited undigested food and dark blood while at school the previous day; she had no other symptoms beyond some vague abdominal pain and nausea for two days prior to the haematemesis.

ON EXAMINATION she was pale, but her general condition was good. Slight epigastric tenderness was the only abnormal clinical finding. The liver and spleen were not palpable. There were no enlarged glands. Immediately after examination she vomited four ounces of dark blood.

BLOOD COUNTS: FEBRUARY 14, 1936. Hb. 68 per cent., red cells 3,420,000 per c.mm., colour index 1.0, white cells 6,450 per c.mm., polymorphs. 45 per cent., lymphocytes 52 per cent., monocytes 3 per cent. Film appearance: red cells showed slight anisocytosis and poikilocytosis. No immature red or white cells seen. Platelets appeared in normal numbers. FEBRUARY 24, 1936: Hb. 65 per cent., red cells 3,280,000, colour index 1.0, white cells 9,800, in normal proportions. Platelets 192,150.

There were no further symptoms while in hospital. She was discharged on March 4, 1936, and attended as out-patient. She was last seen April 16, 1936, having had no further symptoms. The liver and spleen were not palpable.

BLOOD COUNT APRIL 8, 1936: Hb. 87 per cent., red cells, 4,950,000, white cells 6,000.

This case comes under the heading of splenic anaemia, due to a vascular disturbance—possibly thrombophlebitis of the splenic vein as described by Smith and Howard. The haematemesis without warning, impalpable spleen and no definite leucopenia fit in with their description although the spleen had not become palpable two months after the haematemesis. The fact that the usual leucocytosis did not occur after a haemorrhage strengthens the view that the case is one of splenic anaemia. The case illustrates the point that haematemesis occurs in the absence of hepatic cirrhosis and associated gastric or oesophageal varices, of which there was no evidence; the source of bleeding is presumably leakage from distended vasa brevia. Time alone will show whether the diagnosis is correct and whether the full syndrome develops after a presumed vascular accident in the portal system.

Case 2. D. L., a girl, aged 11 years, had attended the Hospital for Sick Children, Great Ormond Street, since July 30, 1935, complaining of bilious attacks for the previous two to three years and capricious appetite. At that time the spleen was enlarged by two fingers breadth and the liver was not palpable. She was admitted for investigation in October, 1935.

BLOOD COUNT: Hb. 85 per cent., red cells 5,000,000, colour index, 0.85, white cells 5,000, in normal proportions.

The Wassermann and van den Bergh reactions were negative. Fragility of red cells and test meal were normal. She was discharged November 11, 1935, and attended as out-patient.

She continued to attend as an out-patient and in December, 1935, the spleen was noticed to be larger. There were no more 'liverish' attacks. In February, 1936, the spleen was a little larger. In March, 1936, the liver was noticed to be definitely enlarged, especially the left lobe. She was admitted to the Middlesex Hospital.

ON EXAMINATION. She had a good colour. The spleen was greatly enlarged extending down left loin almost to iliac crest. The liver was enlarged and firm. There were no other abnormal findings.

BLOOD COUNT, MAY, 12, 1936: Hb. 110 per cent., red cells, 5,420,000, white cells 5,950, polymorphs. 41 per cent., lymphocytes 54 per cent., monocytes 2 per cent., eosinophils 3 per cent., platelets 210,000, reticulocytes 2 per cent. Film appearances: red cells were regular in size and shape but showed some polychromasia. No immature red or white cells were seen.

MARCH 29, 1936. Splenectomy by Mr. D. H. Patey. The spleen was much enlarged, with adhesions to the diaphragm. The liver was seen to be enlarged and hard and its surface had a red and yellow mottled appearance but was not nodular. There was no ascites. The weight of the spleen was 274 gm. A small post-operative blood transfusion was given.

HISTOLOGY OF SPLEEN. There was relative diminution of lymphoid tissue associated with thickening of the walls of the sinusoids and hyaline degeneration of arterioles. Diffuse fibrosis of splenic pulp was present.

Convalescence was eventful. The patient was discharged June 19, 1936, with a blood count of Hb. 102 per cent., red cells 4,980,000, white cells 11,600 and platelets 519,000.

This case is classified under Banti's disease, since there is no known etiological factor present. There is reliable evidence of marked splenomegaly associated with 'bilious attacks,' followed by progressive enlargement of the liver—from being impalpable in July, 1935, to being much enlarged in May, 1936. At operation the liver was considered to be in a pre-cirrhotic state; the spleen showed the histological appearance of Banti's disease and sections of the splenic vein revealed no abnormality. The importance of this case lies in the fact that splenomegaly was present for a considerable time before the liver enlarged, thus corresponding to Banti's original suggestion of a primary splenic cause. The absence of either haemorrhage or anaemia suggests that the latter may depend more on the former than any primary splenic dysfunction.

Case 3. L. B., a girl aged 10 years was admitted to the Middlesex Hospital, May 1, 1936. She had her first haematemesis at the age of 18 months for which she was admitted to King Edward VII Hospital, Windsor. There the Wassermann was negative and she was diagnosed as a case of von Jaksch's anaemia and rickets. At the age of 5 years she had another haematemesis and she was re-admitted to Windsor, where her Hb. was 28 per cent. She had repeated haematemeses and melaena in April, 1936, for which she was re-admitted to Windsor. There her Hb. was 50 per cent. and she received a blood transfusion. She was transferred to the Middlesex Hospital after this.

ON EXAMINATION she was very pale. The spleen was firm and enlarged to two fingers breadth below the costal margin. The liver was enlarged one finger breadth. There was no ascites or enlarged glands.

BLOOD COUNT, MAY 4, 1936: Hb. 25 per cent., red cells 1,780,000, colour index 0.7, white cells 2,200, polymorphs. 56 per cent., lymphocytes 40 per cent., monocytes 3 per cent., eosinophils 1 per cent., platelets 84,700. Film appearances: red cells showed marked anisocytosis, poikilocytosis and polychromasia. No immature red or white cells seen.

MAY 13, 1936. Splenectomy by Mr. E. L. Pearce Gould. The spleen was much enlarged with many adhesions to the diaphragm. Definite coarse cirrhosis of the liver was observed. The weight of the spleen was 310 gm. A drip-blood transfusion during and after operation was given.

HISTOLOGY OF SPLEEN. Some diminution of lymphoid tissue was present with dense fibrosis of the walls of the sinusoids and periarterial fibrosis of the Malpighian arterioles. Diffuse fibrosis of the splenic pulp was also noted.

Her convalescence was uneventful. She was discharged June 4, 1936.

BLOOD COUNT, AUGUST 29, 1936: Hb. 84 per cent., red cells 4,330,000, white cells 5,020. The mother stated that the child had passed black motions occasionally since discharge.

This case, in which there is also no known etiological factor, illustrates fully-developed Banti's disease with the exception of ascites. The repeated haematemeses over a period of eight-and-a-half years are typical as regards length of time, but must be almost unique in having started at the age of eighteen months. It is possible that some vascular accident occurred in

the portal system at that time, but no histological evidence of it remains in the splenic vein, and the appearances of the spleen are typical of Banti's disease. A secondary anaemia is to be expected after recent severe haematemeses—despite transfusion—while the leucopenia, even after haemorrhages, and the thrombocytopenia are typical. The fact that the child was diagnosed as von Jaksch's anaemia at eighteen months suggests that she had splenomegaly if not hepatomegaly, at that time. The subsequent course of this patient will be interesting from the aspect of possible haematemeses after splenectomy, and whether operation will have prevented advance of the cirrhosis and onset of ascites or not.

Case 4. W. F., a girl, aged 8 years, was admitted, January, 1935, to Addenbrooke's Hospital, Cambridge, under Dr. Leslie Cole, complaining of jaundice and abdominal enlargement. She had had 'yellow jaundice' two years before admission, which had persisted since.

ON EXAMINATION there was a definite icteric tint of skin and conjunctivae. The spleen was enlarged three finger breadths, and the liver was enlarged two finger breadths below the costal margin. Eversion of umbilicus was present and distension of abdomen by ascites. Three small glands were palpable in right axilla and a few in both sternomastoid chains. There were several carious teeth.

BLOOD COUNT: Hb. 70 per cent., red cells 4,460,000, colour index 0.79, white cells 8,400, polymorphs 28 per cent., lymphocytes 68 per cent., monocytes 3 per cent., eosinophils 1 per cent. Film appearances—red cells regular in size and shape, no immature red or white cells seen. Fragility of red cells (Dr. C. H. Whittle) 'Haemolysis commences at 0.38 per cent. saline and is only 60 per cent. complete in 0.28 per cent. saline, i.e., less fragile than normal.' The van den Bergh reaction was indirect positive. The Wassermann reaction was 0/±000. The child was then given a provocative dose of 0.18 gm. sulpharsenol intramuscularly and one week later the reaction read 0/+++0. She was discharged and attended as an out-patient for anti-syphilitic treatment. The child was shown at a meeting of the Section for the Study of Disease in Childhood of the Royal Society of Medicine at Addenbrooke's Hospital, Cambridge, on June 27, 1936, seventeen months later. Her general condition was good, she had been at school since discharge from hospital and had had no further attacks of jaundice. On examination there was no ascites, the liver was just palpable only, while the spleen was about the same size. The Wassermann reaction was 0/0000.

BLOOD COUNT, JUNE 9, 1936: Hb. 70 per cent., red cells 4,350,000, colour index 0.8, white cells 8,600, polymorphs 53 per cent., lymphocytes 41 per cent., monocytes 4 per cent., eosinophils 2 per cent.

This case exhibited the clinical features of Banti's ascitic stage; the few small palpable glands alone were atypical, the cervical ones were attributed to the carious teeth. The absence of a definite leucopenia at such an apparently late stage of Banti's disease in addition to the long history of jaundice was, however, a warning that the case was not entirely

typical. The diagnosis of congenital syphilis can be justifiably criticized in this case on the grounds that the Wassermann is usually more than a weak positive in congenital disease and only becomes negative after prolonged treatment; further the child showed no syphilitic stigmata and the Wassermann reactions of her mother and small brother were negative. Despite these considerations there can hardly be any other diagnosis in the face of such dramatic and rapid response to antisyphilitic treatment; namely disappearance of long-standing jaundice, and ascites associated with an enlarged liver clinically simulating hepatic cirrhosis. Although, in theory, a positive Wassermann from non-specific causes might increase in strength with non-specific provocative therapy, in practice this is not proven and a reaction raised by provocative therapy is generally accepted as evidence of syphilis. The case is a fine example of the way in which other conditions can mimic Banti's disease, and emphasizes the care needed in diagnosis, especially to avoid unnecessary splenectomy—an operation which carries a definite mortality at any age.

General discussion.

Banti's disease is said to be rare in children. Poynton, Thurstfield and Paterson¹¹ doubted if it occurred before puberty and could recall few cases in which subsequent events upheld the diagnosis, either syphilis, tuberculosis or acholuric jaundice being later recognized. The diagnosis of Banti's disease is seldom made before one of the major symptoms, such as haematemesis or grave anaemia, has occurred although examination of a child with a vague epigastric pain or swelling of the abdomen may reveal an enlarged spleen and a palpable liver. All conditions associated with splenomegaly in childhood must be excluded, and it must be remembered that the haemopoietic system of a child is unstable and reacts violently to stimuli which would have little or no effect upon an adult. The reaction may take the form of splenomegaly, hepatomegaly, enlargement of lymphatic glands and varying degrees of anaemia—such as occurs typically in von Jaksch's syndrome in response to stimuli like iron deficiency, rickets and syphilis or other infections. The two most important conditions to be excluded before diagnosing Banti's disease are syphilis and acholuric jaundice. Syphilis may exactly simulate Banti's disease, as in case 4, and hepatomegaly may accompany splenomegaly in acholuric jaundice—hence the Wassermann reaction and fragility of red cells are essential investigations. Small doses of iron, as a therapeutic test, may help to exclude an iron deficiency anaemia—but massive doses should not be given in view of Davidson's⁵ successes in the treatment of Banti's disease by such doses of iron.

It is suggested, therefore, that the term Banti's disease be confined to those cases showing splenomegaly and secondary anaemia, with or without haemorrhages and hepatic cirrhosis, but in which no known etiological factor is present. Similarly splenic anaemia should be applied to cases showing Banti's syndrome where some vascular disorder or specific infection can be recognized during life. It must be conceded, however, that

the finding of portal or splenic thrombophlebitis at autopsy on a case of Banti's disease, should not nullify the diagnosis made during life, until further work has shown whether such vascular abnormality is a cause or sequel.

Summary.

1. Banti's syndrome, although uncommon, occurs in children.
2. It is suggested that the term Banti's disease be applied to cases exhibiting the syndrome with no known etiological factor.
3. Where certain etiological factors, which are described, can be found, the term splenic anaemia should be used.
4. Four cases exhibiting Banti's syndrome are described and discussed.

Appendix.

ANALYSIS OF HAEMATOLOGICAL INVESTIGATIONS.

1. RED CELLS AND HAEMOGLOBIN ON ADMISSION.

CASE	Hb. PER CENT.	R.B.C. MILLS. PER C.MM.	C. INDEX	FILM APPEARANCES.
1	68	3.42	1.0	SLIGHT ANISOCYTOSIS AND POIKILOCYTOSIS.
2	85	5.00	0.85	SOME POLYCHROMASIA.
3	25	1.78	0.7	MARKED ANISOCYTOSIS, POIKILOCYTOSIS AND POLYCHROMASIA.
4	70	4.46	0.79	CELLS REGULAR.

Cases 1, 3 and 4 showed anaemia, with anisocytosis and poikilocytosis as might be expected in cases 1 and 3 after recent haematemesis.

2. WHITE CELLS ON ADMISSION.

CASE	W.B.C. THOUS. PER C.MM.	POLY. PER CENT.	LYMPHS. PER CENT.	MONO. PER CENT.	EOSIN. PER CENT.
1	6,450	45	52	3	-
2	5,950	41	54	2	3
3	2,200	56	40	3	1
4	8,400	28	68	3	1

Cases 1, 2 and 3 showed leucopenia, marked in case 3 and slight in cases 1 and 2. The polymorph percentage is low for children of these ages.

Absence of the usual leucocytosis following haemorrhage in cases 1 and 3 is a point of some importance; in a larger series of adult cases of Banti's disease the persistent leucopenia after haematemesis has been contrasted with the leucocytosis which occurs after haemorrhage from other causes. King⁸, however, emphasized a leucopenia occurring in hepatic cirrhosis and maintained that it could not be used as a differential point between Banti's disease and portal cirrhosis in adults.

3. PLATELETS.

CASE	PLATELETS ON ADMISSION PER C.MM.	14 DAYS AFTER OPERATION	26 DAYS AFTER OPERATION
1	192,150	—	—
2	220,000	519,000	—
3	84,700	290,000	553,000
4	90,000	—	—

Cases 1, 3 and 4 showed low platelet counts and cases 2 and 3, who were subjected to splenectomy, showed the striking post-operative rise described by Rosenthal¹² and Howel Evans⁶.

4. FRAGILITY OF RED CELLS.

In cases 1, 2 and 3 the fragility of red cells was normal—no haemolysis occurring at a saline concentration greater than 0.5 per cent. In case 4 the red cells were less fragile than normal—haemolysis beginning at 0.38 per cent. saline and being only 60 per cent. complete in 0.28 per cent. saline (Dr. C. H. Whittle). Whitby and Hynes¹⁶ mentioned the scarcity of literature on the subject of decreased red cell fragility, but gave particulars of four cases in which it had occurred following splenectomy for purpura haemorrhagica or acholuric jaundice. Fragility is also said to be decreased in pernicious anaemia, cachectic states and sickle-celled anaemia.

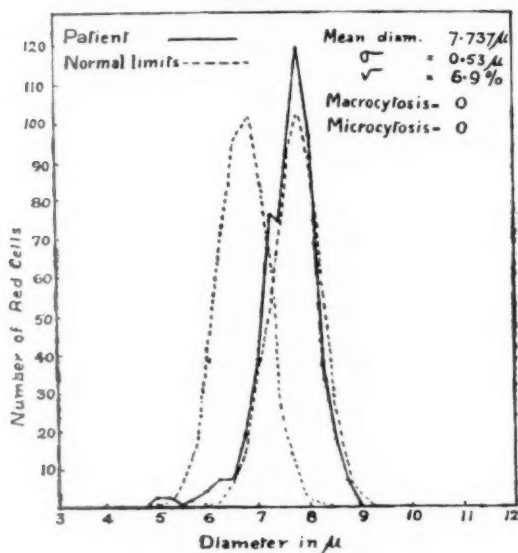
In case 4 the syphilitic infection may be the causal factor.

5. BLOOD INDICES AND ABSOLUTE DETERMINATIONS.

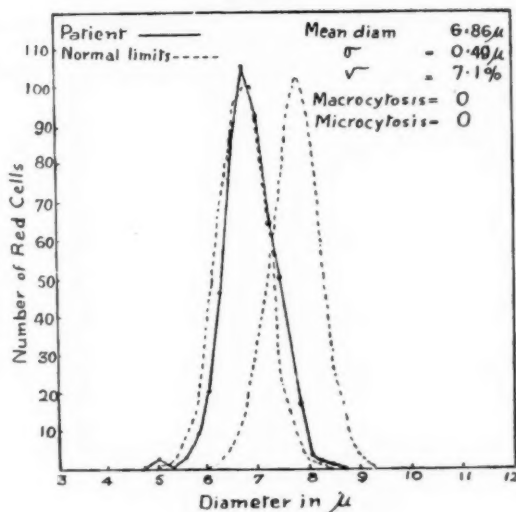
	NORMAL	CASES			
		1	2	3	4
VOLUME INDEX ...	0.95-1.05	1.15	0.92	0.83	0.98
SATURATION INDEX ...	0.9-1.2	0.93	1.0	0.7	0.76
MEAN CORPUSCULAR Hb.	27-32%	34	28	18	22
MEAN CORPUSCULAR VOL.	80-94 CU. μ	99	79	72	84
MEAN CORPUSCULAR Hb. CONC.	33-38 PER. CENT.	31	35	24	27
MEAN CORPUSCULAR THICKNESS	1.8-2.2 μ	2.1	2.15	1.75	2.18

6. PRICE-JONES DIAMETER-DISTRIBUTION CURVES OF RED CELLS by the technique of Hynes and Martin⁷ show no gross or characteristic departure from the normal.

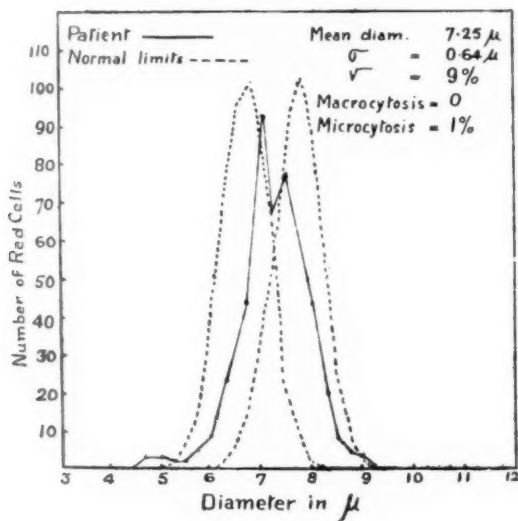
Case 1.



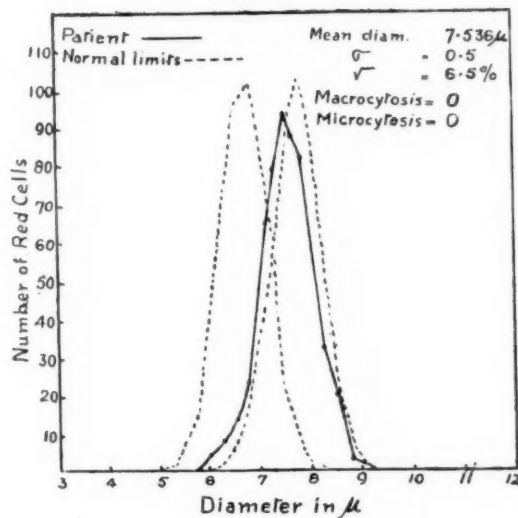
Case 2.



Case 3.



Case 4.



	NORMAL	CASES			
		1	2	3	4
STANDARD DEVIATION	0.4-0.5 μ	0.53	0.49	0.64	0.50
COEFFICIENT OF VARIATION	5.3-7.3 PER. CENT.	6.9	7.1	9.0	6.5
MACROCYTOSIS ...	0	0	0	0	0
MICROCYTOSIS ...	0	0	0	1 PER CENT.	0
MEAN CELL DIAMETER	6.69-7.72 μ	7.73	6.86	7.25	7.53

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THE OSSIFICATION OF THE CARPUS IN RICKETS, CONGENITAL SYPHILIS AND CRETINISM

BY

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It is generally believed that in rickets and cretinism there is delay in the appearance of the centres of ossification of the carpus, and some hold that there is a similar delay in congenital syphilis (Köhler⁶, Holmes and Ruggles¹). Recently Signorelli, Hosen and Miles⁹ have claimed that in rickets and congenital syphilis the time of appearance of these centres is normal.

In view of these contradictory findings the records of children admitted to the Royal Hospital for Sick Children during the last ten years suffering from these diseases were examined. In each case the diagnosis was established clinically and by skiagrams. The case reports and x-ray plates of 211 cases of active rickets under five years of age, fourteen cases of congenital syphilis and twenty of cretinism were examined.

Before studying the available material it was first necessary to establish a standard of normality. On investigating the literature on the subject it was found that there was considerable variation among the different

TABLE 1.

	Female.	Male.
Capitate	3 - 6 months	4 - 10 months
Hamate	5 - 10 "	6 - 12 "
Triquetral	2 - 3 years	About 3 years
Lunate	3 - 4 "	" 4 "
Navicular	4 - 5 "	4 - 5 years
Trapezoid	4 - 5 "	5 - 6 "
Trapezium	4 - 5 "	5 - 6 "
Pisiform	9 - 10 "	12 - 13 "
Radial Epiphysis	About 8 months	About 15 months
Ulnar Epiphysis	5 - 7 years	6 - 8 years
First Metacarpal	Early 3rd year	2 - 3 "

PRYOR'S STANDARD OF NORMAL OSSIFICATION OF THE CARPUS.

authorities regarding the age at which the carpal centres appear in the normal child. Pryor's⁷ tables, though old, are accurate, detailed and comprehensive and are based on radiological examination. They differ in some respects from the anatomical tables of Quain⁸, Debieyre¹ and Gray³ and from those of Feer¹⁰, Holt and McIntosh⁵, and Fujinami¹², all based on radiological evidence and from a table compiled from examination of a large number of x-ray plates of normal wrists at the Royal Hospital for Sick Children. To overcome this difficulty two tables were utilized, viz., that compiled by Pryor⁷ (table 1) and a composite table constructed from the standards of normality suggested by the other workers mentioned above (table 2). In both these tables the age at which the lower epiphyseal centres

TABLE 2.

Capitate	Birth to 1 year
Hamate	Birth to 1 year
Triquetral	2 to 3½ years
Lunate	3 to 5½ "
Trapezium	4 to 5½ "
Trapezoid	4 to 6 "
Navicular	5 to 6 "
Pisiform	10 to 12 "
Radial Epiphysis	1 to 2½ "
Ulnar Epiphysis	4 to 7 "
First Metacarpal	2 to 3 "

COMPOSITE STANDARD OF NORMAL OSSIFICATION COMPILED FROM QUAIN, FEER, DEBIERRE, HOLT AND MCINTOSH, FUJINAMI, GRAY, PRYOR AND ROYAL HOSPITAL FOR SICK CHILDREN RECORDS.

of the radius and ulna and the epiphyseal centre of the first metacarpal appeared were included. The pathological series here presented was compared with both these standards. When using Pryor's tables the differences in ossification in the two sexes were taken into consideration, but in comparing this material with the composite table, sex has been disregarded as no data are available.

Applying Pryor's standard, table 3 shows the number of cases in this series showing advanced, normal or delayed ossification in the three diseases

TABLE 3.

Rickets	Advanced	18 (9 per cent.)
				Normal	141 (66 " ")
				Delayed	52 (25 " ")
Congenital syphilis	Advanced	7
				Normal	6
				Delayed	1
Cretinism	Advanced	0
				Normal	0
				Delayed	20

OSSIFICATION OF CARPUS IN RICKETS, CONGENITAL SYPHILIS AND CRETINISM COMPARED WITH PRYOR'S STANDARD.

under consideration, while table 4 gives the results when compared with the composite standard. In the latter the range of normality is wide and consequently a larger number appear to show normal ossification. The difference in the number of cases appearing in the two tables is due to the fact that with the composite standard it is impossible to determine whether there is any retardation in the appearance of the centres till the patient reaches the age of one year, while, using Pryor's table, it is possible to detect delay after the age of six months.

TABLE 4.

Rickets	Advanced	13 (6 per cent.)
	Normal	150 (73 " ")
	Delayed	44 (21 " ")
Congenital syphilis	Advanced	2
	Normal	11
	Delayed	0
Cretinism	Advanced	0
	Normal	1
	Delayed	15

OSSIFICATION OF CARPUS IN RICKETS, CONGENITAL SYPHILIS AND CRETINISM
COMPARED WITH COMPOSITE STANDARD.

Both comparisons, however, show a similar result for each disease. In at least 75 per cent. of the cases of rickets ossification was normal or advanced and only in about 25 per cent. was it delayed. In the congenital syphilis series only one case showed delay in ossification and this was only apparent with Pryor's standard. In cretinism, on the other hand, there was delay in all the cases save one and that only when compared to the composite scale which is a less exacting standard than that of Pryor. On the whole the present results are in accord with the findings of Signorelli and his co-workers⁹. In one respect, however, they are not in agreement with their conclusions, namely, that the late appearance of the carpal centres is in itself diagnostic of cretinism, for in about 25 per cent. of the present cases of rickets the centres of ossification have appeared late.

No explanation has been found to account for this delay. The patients showed the characteristic bony changes of rickets and none of the signs of cretinism, and at no particular age was the retardation specially manifest; for, when the cases were classified in age groups, the tendency to delay was no more marked in one group than in another. The question whether severe deficiency in the phosphorus content of the blood might afford an explanation of the delay was also taken into consideration. As the phosphorus had been estimated in a large number of cases the state of ossification was compared with the biochemical findings. From this it appeared that while on the whole there was a parallelism between the degree of reduction in serum phosphorus and the extent of the delay in ossification this was not always the case; in some cases with delayed ossification and active rickets as shown by x-ray, the phosphorus content of the serum was

normal. This, however, may be due to the fact that the phosphorus may rise to the normal level within a few weeks from the beginning of treatment while the radiological signs of calcification take longer to appear.

Summary.

These records indicate that ossification is almost invariably delayed in cretinism, frequently advanced and seldom delayed in congenital syphilis and delayed in about 25 per cent. of cases of rickets. In view of the delay in the appearance of the carpal centres of ossification in some cases of rickets without any signs of hypothyroidism it does not seem justifiable to claim that this is in itself diagnostic of congenital thyroid deficiency.

Acknowledgement and thanks are due to Dr. Leonard Findlay and the present members of the staff for permission to use their case records and for much helpful advice and criticism.

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THE BLOOD-SUGAR IN CONVULSIONS OF INFANCY AND CHILDHOOD

BY

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It has long been recognized that severe convulsive attacks are followed by depletion of the carbohydrate reserves of the body. Indeed one of the experimental methods of exhausting the glycogen of the tissues is by inducing convulsions by the administration of strychnine or other similar drugs. Clearly in these circumstances the reduction of available carbohydrate is the result and not the cause of the convulsion. Following on the recognition of hyperinsulinism as a cause of convulsions, however, the possibility has arisen that hypoglycaemia may be an etiological factor in the production of convulsions in infancy and childhood and there is no doubt that convulsions due to this occasionally occur.

Two cases have been recorded by Kramer, Grayzel and Solomon¹, and Josephs^{2,3} has suggested that the combination of fever and a short fast may produce a state of hypoglycaemia which may explain the convulsions occurring at the onset of an acute infection. Other workers, however, while noting the presence of hypoglycaemia in the post-convulsive state have hesitated to attribute the seizure to the disturbance in carbohydrate metabolism. Griffiths⁴ noted the association of hypoglycaemia with convulsions but was not sure whether the low blood-sugar was the cause, the result or merely coincident with the convulsion. Higgins⁵ observed hypoglycaemia following convulsions in two new-born babies. Fleming, Herring and Morris⁶ reported three patients who were admitted to hospital comatose and had either glycosuria or a raised blood-sugar which in two of them was followed by hypoglycaemia, and Darrow⁷ recently reported two examples of recurring convulsions in mentally defective children in whom hypoglycaemia was frequently noted but on two occasions shortly after a convulsion the blood-sugar was found to be high. It was found that in the hypoglycaemic phase these children did not respond well to glucose.

The suggestion that idiopathic or epileptic convulsions of infancy and childhood are caused by a state of hypoglycaemia at first sight seems unlikely, for true hypoglycaemic convulsions arising, for example, from over-dosage with or from an excessive production of insulin are of a different nature from the ordinary convulsions of childhood. Frequently the hypoglycaemic fit is preceded by a period of fatigue, malaise, hunger, fear, negativism, confused speech and automatism—none of which is a feature of convulsions due to other causes. While the convulsion itself is indistinguishable from any other, these prodromal symptoms as well as the ready and complete recovery following the administration of

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adrenaline or glucose seem to differentiate such seizures. Much that is equivocal has been written on the sugar content of the blood in idiopathic epilepsy.

Daly, Pryde and Walker⁸ thought there might be some relationship between low values and the onset of seizures but found the results inconclusive. Lennox and Cobb⁹, after examining a large number of cases, came to the conclusion that the great majority of epileptics presented no disturbance of carbohydrate metabolism and that any change in the sugar content of the blood following a convulsion was merely the result of the increased muscular exertion and the asphyxia. Nielsen¹⁰, on the other hand, found that about 90 per cent. of cases of idiopathic epilepsy showed a tendency to hypoglycaemia though he did not consider that hypoglycaemia alone was sufficient to precipitate an attack. This contention was supported by Tyson, Otis and Joyce¹¹, who found a tendency in epileptics as a whole towards subnormal fasting blood-sugar values. These authorities drew their conclusions from the study of sugar tolerance curves in epileptics and paid less attention to the blood-sugar level during or shortly after a convulsion.

Present investigation

In view of the confusion of opinion regarding the rôle of hypoglycaemia in the etiology of convulsions in childhood, blood-sugar estimations were made in a series of children admitted to hospital on account of convulsions and an attempt was made to follow the changes occurring in the blood-sugar level from the beginning of a convulsion till some hours after it had ceased. Unfortunately it was never possible to obtain a blood-sugar reading immediately before a convulsion. The patients were of ages varying from two days to eleven-and-a-half years and the seizures were due to various causes, such as birth injury, spasmophilia, meningitis, epilepsy or acute infections. The blood-sugar was estimated by a modified Folin and Wu method.

Fifty patients were examined and of these three were examined on two separate occasions making in all fifty-three observations. The blood-sugar was estimated at frequent intervals—often hourly. The results are given in an abbreviated form in table 1. This shows the maximum and minimum blood-sugar values during four periods, (1) from the onset until three hours, (2) from the fourth till the twelfth hour, (3) from the thirteenth till the twenty-fourth hour and (4) from the twenty-fourth till the forty-eight hour after the convulsion. It will be seen that high blood-sugar values occur most frequently in the first three hours after the convulsion and that these often persist into the second period. The hypoglycaemic readings are scattered throughout the last three periods but occur most frequently in the second of these. It appears, therefore, that there are as a general rule two phases, a state of hyperglycaemia followed by one of hypoglycaemia. A blood-sugar level of more than 180 mgm. per cent. was taken as indicating hyperglycaemia and one of less than 60 mgm. per cent. as hypoglycaemia. The following is a typical case (case 16).

E. F., a girl, aged one-and-a-half years, was delivered by Caesarean section and appeared healthy at birth. She thrived and developed normally and had always been healthy except for an attack

TABLE 1.

MAXIMUM AND MINIMUM BLOOD-SUGAR READINGS AFTER CONVULSIONS.

No.	NAME.	AGE.	0-3 HOURS.			4-12 HOURS.			13-24 HOURS.			25-48 HOURS.			DIAGNOSIS.
			MAX. PER CENT.	MIN. PER CENT.	MGM.	MAX. PER CENT.	MIN. PER CENT.	MGM.	MAX. PER CENT.	MIN. PER CENT.	MGM.	MAX. PER CENT.	MIN. PER CENT.	MGM.	
1	M. G.	10½ mth.	250	188.7	144.9	98.8	81.9	112.3	77.5	46.9	—	47.6	—	—	Tub. meningitis
2	D. McL.	5 yr. 1 mth.	—	—	—	57.4	44.4	—	55.5	36.5	—	—	—	44.6	Tub. kidney; ? cerebral tuberculoma
3	H. K.	5 yr. 3 mth.	—	317.4	—	—	—	—	—	—	—	—	69.5	—	P.U.O.
4	W. McK.	2 yr. 1 mth.	—	—	—	253.2	89.3	—	111.1	87.7	—	—	—	—	Nasal diphtheria
5	M. McL.	18 wk.	476.1	303.0	—	158.7	105.2	—	121.9	80.6	—	144.9	91.8	—	Tub. meningitis
6	W. M.	8 yr.	133.3	85.4	—	104.1	91.8	—	112.3	75.2	—	—	66.6	—	?
7	G. W.	2 yr. 3 mth.	—	—	—	73.5	36.3	—	—	—	—	75.2	49.7	—	? Tetany
8	C. M.	1 yr. 1 mth.	133.3	75.2	—	—	—	—	78.1	71.9	—	—	—	—	Tetany
9	J. McL.	21 wk.	—	—	—	—	—	—	—	—	—	89.3	62.1	—	Tetany
10	A. M.	11 wk.	277.7	238.1	—	—	152.6	—	135.1	90.9	—	—	—	—	Anaemia
11	A. M.	5 yr. 8 mth.	303.0	119.0	—	—	—	—	—	—	—	—	—	—	Tub. meningitis
12	E. M.	3 yr. 2 mth.	196.1	88.5	—	—	—	—	—	—	—	119.0	52.6	—	Miliary tub.
13	D. R.	2 yr. 5 mth.	188.7	126.5	—	232.5	126.5	—	103.1	59.1	—	—	—	—	Epilepsy
14	J. C.	8 yr. 8 mth.	156.2	129.8	—	178.6	60.6	—	97.1	95.2	—	—	—	—	Tub. meningitis
15	A. H.	1 yr. 3 mth.	158.7	131.6	—	116.2	90.9	—	82.2	71.9	—	—	—	—	Epilepsy
16	E. F.	11 yr. 6 mth.	140.8	95.2	—	120.5	102.0	—	—	—	—	—	—	—	? Epilepsy
17	T. B.	1 yr. 6 mth.	232.6	149.7	—	144.9	42.8	—	—	—	—	—	—	—	Pneumonia
18	A. McM.	1 yr. 6 mth.	—	—	—	88.5	81.3	136.9	144.9	56.2	—	109.9	99.0	—	Tetany
19	B. T.	10 mth.	—	—	—	60.9	—	—	62.2	45.8	—	90.1	67.1	—	Intracranial birth injury
20	A. G.	2 days	—	—	—	39.8	—	—	—	—	—	50.2	42.0	—	Intracranial birth injury
21	E. G.	3 days	250.0	204.1	—	—	—	—	55.5	42.6	36.7	—	—	—	?
22	J. H.	1 yr. 11 mth.	—	—	—	125.0	52.0	—	—	—	—	69.4	40.9	—	Gastro-enteritis
23	A. P.	2 yr. 2 mth.	—	—	—	59.5	49.5	—	94.3	79.7	—	—	—	—	Gastro-enteritis
		5 wk.	—	—	—	—	—	—	—	—	—	—	—	—	
		18 wk.	—	—	—	21.0	3.7	—	—	—	—	—	—	—	

TABLE 1—continued.

No.	NAME.	AGE.	0-3 HOURS.		4-12 HOURS.		13-24 HOURS.		25-48 HOURS.		DIAGNOSIS.
			MAX. MGM. PER CENT.	MIN. MGM. PER CENT.	MAX. MGM. PER CENT.	MIN. MGM. PER CENT.	MAX. MGM. PER CENT.	MIN. MGM. PER CENT.	MAX. MGM. PER CENT.	MIN. MGM. PER CENT.	
24	J. G.	2 yrs.	—	—	21.0	18.8	—	—	—	—	Broncho-pneumonia
25	J. C.	2 days	—	—	—	—	—	—	—	—	Intracranial birth injury
26	M. McA.	9 wk.	—	—	—	—	46.5	—	—	—	Gastro-enteritis
27	D. N.	3 days	—	—	—	—	—	—	—	—	Intracranial birth injury
28	V. C.	6 wk.	—	—	—	—	—	—	25.2	—	Gastro-enteritis
29	J. R.	7 mth.	103.1	33.0	21.0	18.8	—	—	—	—	Ileo colitis
30	J. W.	2 mth.	250.0	169.5	—	—	—	—	—	—	Tub. meningitis
31	M. C.	12 days	—	—	—	—	—	—	—	—	Intracranial birth injury
32	M. G.	4 mth.	—	—	—	—	—	—	—	—	Tub. meningitis
33	T. M.	3 mth.	—	—	—	—	—	—	—	—	Tub. meningitis
34	O. McC.	3 yr. 11 mth.	—	—	—	—	—	—	—	—	? Tetany
35	E. S.	8 wk.	—	—	63.3	—	—	—	—	—	German measles
36	W. M.	27 wk.	—	—	104.1	92.6	—	—	112.3	—	Tetany
37	M. O'H.	10 yr.	—	—	—	—	—	—	—	—	Nephritis
38	E. W.	4 mth.	97.1	90.1	—	—	78.7	72.4	97.1	58.5	Tub. meningitis
39	C. O.	11 yr.	102.2	95.2	97.1	91.7	—	—	—	—	Epilepsy
40	M. H.	11 yr.	86.9	71.9	94.7	—	—	—	—	—	? Tuberculoma of brain
41	C. S.	1 yr. 10 mth.	86.2	77.5	86.9	76.3	82.6	65.6	—	—	Tetany
42	R. D.	5 yr.	—	96.1	95.2	68.9	105.3	78.1	109.2	80.0	? Epilepsy
43	J. W.	6 yr. 10 mth.	—	—	120.5	93.4	89.3	—	112.3	85.5	Epilepsy
44	D. M.	1 yr. 11 mth.	—	—	100.0	98.4	140.8	66.2	113.6	93.4	Tonsillitis
45	P. C.	7 wk.	—	—	95.2	61.7	119.0	90.1	108.7	79.4	? Tetany
46	C. S.	15 mth.	80.0	78.1	102.0	87.7	—	—	79.4	—	Tetany
47	O. M.	1 mth.	—	—	50.0	23.7	66.6	—	—	—	Intracranial birth injury
48	C. McA.	14 wk.	204.1	162.6	204.1	72.9	—	—	—	—	Anaemia
49	M. M.	8½ yr.	94.3	76.3	—	—	105.2	63.7	—	—	Uraemia
50	D. McL.	1 yr. 1 mth.	81.3	—	—	59.5	112.3	81.9	—	—	?

of chicken-pox six months before admission. During the night before admission to hospital she vomited once and slept badly. At 6 a.m. on the day of admission she was found unconscious and from then until she was admitted to hospital had frequent attacks of generalized rigidity each lasting for about five minutes. On admission at 8.30 a.m. she was still unconscious and breathing stertorously. She was a small, pale child and on examination no abnormality was found in the heart, lungs or abdomen. The knee jerks were active and the plantar responses extensor. The rectal temperature was 101.8°. She recovered consciousness at noon but remained drowsy all day. Next day she appeared quite well. The blood-sugar content was estimated at half-hourly intervals for the first few hours and then hourly throughout the day. Some of the readings are shown in table 2.

TABLE 2.

8.45 A.M.	9.45 A.M.	10.45 A.M.	11.45 A.M.	12.45 A.M.	2.15 P.M.	3.15 P.M.	4 P.M.	5 P.M.
232.6	114.9	92.6	74.6	113.6	84.7	58.1	49.5	42.8 mgm. per cent.

At 9 a.m. the next morning the blood-sugar was still rather low, 65.8 mgm. per cent. but by the next day it had risen to a normal level of 89.3 mgm. per cent.

The hyperglycaemic phase

Twenty-six cases were examined within three hours of the onset of a convulsion and eleven of these showed a blood-sugar content above 180 mgm. per cent. In one of the cases this was observed on two occasions (case 12). Fifteen of the patients who were examined within three hours of a convulsion did not show hyperglycaemia but in six the blood-sugar level was over 130 mgm. per cent. and in the remaining nine no value below 80 mgm. was found. In many of these it was impossible to say whether food had recently been taken and on this account the moderate rise observed could not be definitely attributed to the convulsion. Of the cases which did not show hyperglycaemia, three had mild convulsions. This may account for the absence of reaction since the highest blood-sugar readings were usually obtained when the convulsions were severe and prolonged. Further it is probable that the hyperglycaemic state was missed in some of the cases as they were not examined soon enough after the onset of the convulsion. This was almost certainly what occurred in case 43, for urine passed eight-and-a-half hours after the convulsion contained sugar when the blood-sugar content was 78.1 mgm. per cent.

The hypoglycaemic phase

Hypoglycaemia was found at one time or another in twenty-five of the patients. That this was a temporary disturbance is shown by the fact that in three sugar tolerance tests were carried out and in eight others the fasting blood-sugar was estimated during convalescence. In none of these was the curve abnormal or the fasting blood-sugar unduly low. Hypoglycaemia occurred commonly in the second period, i.e., four to twelve

hours after the convulsion but in some at later periods. In one patient (case 29) it occurred in the first period; this was in a child aged nine months, admitted with profound toxæmia due to ileo-colitis. The child had a convulsion on admission to hospital and the blood-sugar then was 103.1 mgm. per cent. She rapidly became moribund and the blood-sugar three hours later had fallen to 33.0 mgm. per cent. The child died four hours after admission to hospital and the blood-sugar immediately after death was found to be 12 mgm. per cent. Low readings below 30 mgm. per cent. were obtained on seven occasions but hypoglycaemic symptoms were never observed. As with the hyperglycaemic phase, the hypoglycaemia, which is often transient, may have occurred in some of the patients in the interval between two observations and consequently may have been missed.

The disturbances in the blood-sugar content described above could not be definitely related to any particular disease nor to any particular type of convulsion; hyperglycaemia, however, seemed to occur most commonly in cases of tuberculous meningitis and intracranial injury in new-born babies seemed most prone to lead to profound hypoglycaemia. Of six cases of meningitis examined within three hours of the convulsion four showed hyperglycaemia and all the six cases of intracranial injury in the series had at one time or another marked hypoglycaemia; five of these infants recovered and in the course of convalescence there was a gradual rise in the blood-sugar to the normal level.

Discussion.

It would appear, therefore, that during or immediately after a convulsion the blood-sugar percentage is frequently raised and that it falls rapidly, sometimes to a low level, remains low for several hours or days and then rises to the normal level. These results confirm the observation of Josephs and others that there is a state of hypoglycaemia following a convulsive attack. Their failure to note the initial rise, except in a few instances, was probably because the observations were, as a rule, not made sufficiently soon after a convulsion to catch the hyperglycaemic phase. The recognition of the biphasic nature of the change provides a possible explanation of its etiology. It seems probable that the initial rise is due to the profound disturbance of the central nervous system occasioned by the convulsion and that this causes mobilization of glucose from glycogen—a condition similar to that produced by Bernard's diabetic puncture.

Titus, Willets and Lightbody¹² noticed a rise in blood-sugar immediately following the convulsions of eclampsia, in some cases slight and in others marked, but concluded that this was only a physiological and transient hyperglycaemia following the strenuous muscular exertion. Romeke and Skouge¹³ have described thirteen cases of cerebral haemorrhage in all of whom there was hyperglycaemia; they suggest that this was caused by over-secretion of adrenaline from stimulation of the medulla oblongata.

In the present series definite hyperglycaemia was only detected in approximately 40 per cent. of the cases examined within three hours of the convulsion. It may be that in a considerable number the hyperglycaemic phase was missed but it is possible that in others the stimulation was

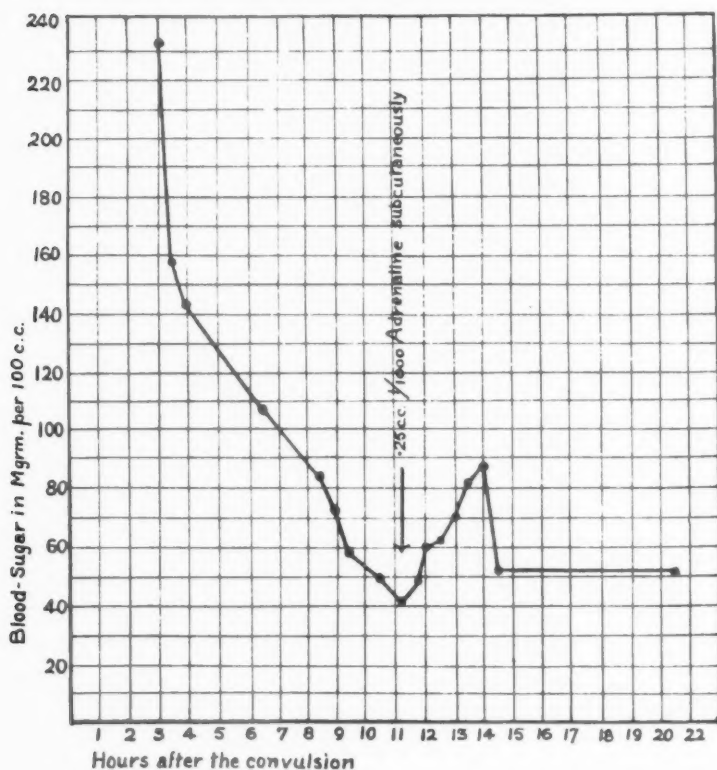
insufficient to affect that part of the brain controlling carbohydrate metabolism.

Regarding the subsequent hypoglycaemic phase there are two possible explanations. It may be that the violent muscular exertion uses all the available carbohydrate and the body tissues are left in a state of carbohydrate depletion or that the central stimulation, acting as it does on the suprarenals, leads to exhaustion of adrenaline and in the absence of this to the cessation of glycogenolysis. Against the first suggestion is the fact that the blood-sugar, though it may show a transient rise after a meal, tends to remain low for many hours after the convulsion even though ample carbohydrate has been given in the food. Moreover it is generally recognized that even during complete starvation the blood-sugar does not fall very appreciably below the fasting level owing to the formation of glucose from endogenous sources, presumably protein and fat. In the patients here described, even though the glycogen stores had been reduced to a low level, which was probably not the case as they all received food, there should not therefore have been hypoglycaemia had there been an adequate stimulus for the production of glucose. Lawrence¹⁴, in a recent paper, has stressed the importance of the adrenal, thyroid and pituitary secretions in 'facilitating the supply of peripheral sugar.' In view of the frequent occurrence of hyperglycaemia prior to the hypoglycaemic phase it seems probable that in many of the present series of patients there was an initial oversecretion with consequent exhaustion of the store of adrenaline. If this reasoning is correct administration of adrenaline should readjust, at any rate temporarily, the level of the blood-sugar. This hypothesis was put to the test on two occasions. Blood-sugar examinations were carried out in the usual way on two children who had had convulsions. When the hypoglycaemic stage was reached adrenaline was injected and the blood-sugar estimations continued at frequent intervals.

The first case in which this procedure was tried was the typical case already described (p. 248). At 5 p.m. when the blood-sugar was 42.8 mgm. per cent., 0.25 c.c. adrenaline (1/1000) was injected subcutaneously. Fig. 1 shows the changes that occurred. It will be seen that there was an immediate response. The blood-sugar rose to over 80 mgm. per cent. within two hours of the injection and within three hours of the beginning of the experiment had fallen to its original level. As the child had been fasting since noon the rise in the blood-sugar cannot be attributed to the taking of food.

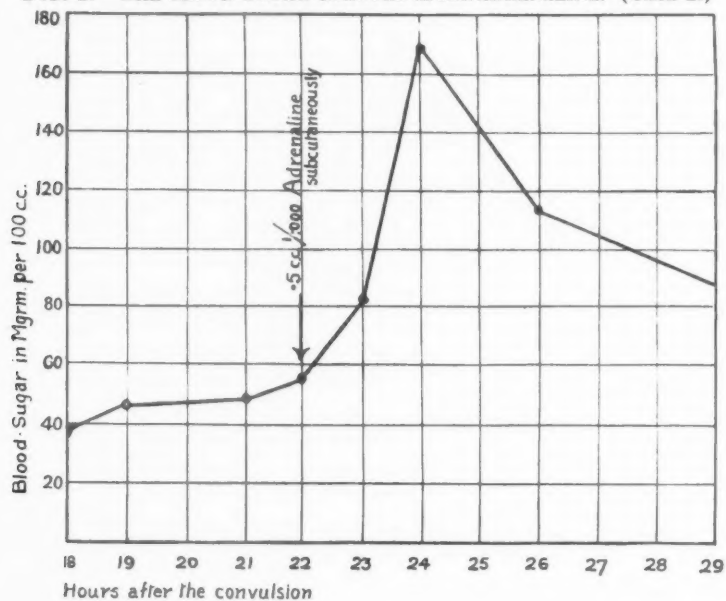
In the second patient (case 2), the initial rise in the blood-sugar level had been missed and observations only began in the hypoglycaemic phase. Some months previously, however, the child had had a similar convulsion and on that occasion the blood-sugar tests had commenced within three hours of the seizure and the hyperglycaemic phase (188.7 mgm. per cent.) had been registered. On the second admission the boy was brought to hospital eighteen hours after a

FIG. 1.—THE BLOOD-SUGAR AFTER ADRENALINE. (CASE 16.)



E. F., aged 1 6/12 years.

FIG. 2.—THE BLOOD-SUGAR CHANGES AFTER ADRENALINE. (CASE 2.)



D. McL., aged 5 3/12 years.

convulsion. At that time he was conscious but drowsy and the blood-sugar level was found to be 36.5 mgm. per cent. There can be little doubt that with the second convulsion there had been a rise similar to that which occurred with the previous convulsion. Fig 2 shows the changes that occurred after giving 0.5 c.c. adrenaline (1/1000) subcutaneously during the hypoglycaemic phase. It will be seen that there was an immediate response, the blood-sugar rising to a level of 169 mgm. one hour forty-five minutes after the injection. No food had been given for at least four hours previous to the adrenaline injection. The response to adrenaline in both cases provides strong evidence in favour of the hypothesis that the hypoglycaemic phase following a convulsion is dependent on deficiency of adrenaline and that, during this period, the tissues are able to form glucose when adrenaline is supplied.

Summary.

1. The blood-sugar content was estimated at frequent intervals after convulsions in fifty children.
2. It was found that when the estimations were done sufficiently soon after a convulsion there was a state of hyperglycaemia in nearly half of the cases.
3. In half the cases a state of hypoglycaemia was found to occur some hours after the convulsion and to persist in spite of taking food.
4. In two cases the administration of adrenaline during the hypoglycaemic phase was followed by a significant rise in the blood-sugar level.
5. The cause of the changes in the blood-sugar concentration is discussed.

Conclusions.

Except in cases of true hyperinsulinism it would appear that hypoglycaemia plays no part in the causation of the convulsions of childhood and that the upset in carbohydrate metabolism is the result and not the cause of the convulsions.

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FURTHER OBSERVATIONS ON ACID METABOLISM IN RHEUMATIC CHILDREN

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In a previous study¹ of this subject, the urinary output of a normal, a rheumatic and an asthmatic group of children was studied. Unfortunately the environment of the normal control group differed from that of the other two groups. Dr. Gray Hill suggested that a group of rheumatic children existed at Queen Mary's Hospital, Carshalton, who were living under identical environmental conditions with the control group. This hospital is within a few miles of the Banstead residential school where the control group lived. The food supply for both is in the same administrative area of the London County Council. The Hospital group had a somewhat higher ration of protein but otherwise the diets were similar. The time of year being of some importance especially when considering food supplies, the same period of time (November to April) was chosen. In the first rheumatic group at the Hospital for Sick Children the patients were all attending the out-patient department and were usually free from symptoms. At Queen Mary's Hospital the majority of the children in the group were well advanced in their convalescence, but a few with some degree of activity were included. An attempt has been made to gauge the effect of the degree of activity by further sub-division of the cases.

The same methods were adopted as before, but in addition in the first 100 cases the estimation of organic acid by simple titration as given by Peters and van Slyke² was performed in order to determine the meaning of the 'non-phosphate acid' values obtained previously. It was found that this value was approximately half the actual organic acid value, 27.98 c.c. per 100 c.c. urine for the 'non-phosphate acid' value as compared with 51.25 c.c. for the Peters-van Slyke organic acid titration. The correlation coefficient indicated a good general agreement between the two sets of values, being $+0.73 \pm 0.0036$, which suggests that the assumption that the 'non-phosphate acid' value gave an indication of the organic acid excretion was justified.

Results.

The following table 1 gives the results obtained compared with the normal control group. The values in the earlier rheumatic group are also given.

TABLE 1.

ESTIMATION	SPECIMEN	RHEUMATIC GROUPS		NORMAL	DIFFERENCES	
		QUEEN MARY'S HOSPITAL	GREAT ORMOND STREET		Q.M.H.- NORMAL	G.O.S.- NORMAL
Free acid	1	16.9 \pm .35	16.9 \pm .44	11.3 \pm .33	5.6 \pm .48	5.6 \pm .55
	2	8.6 \pm .43	10.1 \pm .43	7.5 \pm .31	1.05 \pm .53	2.5 \pm .54
	3	10.0 \pm .39	13.0 \pm .50	9.1 \pm .36	.91 \pm .53	3.9 \pm .61
Total Acid	1	42.26 \pm .65	44.5 \pm .98	31.2 \pm .70	11.1 \pm .95	11.4 \pm 1.18
	2	26.75 \pm .75	32.6 \pm 1.0	24.8 \pm .65	2.0 \pm .99	7.8 \pm 1.21
	3	27.88 \pm .63	34.9 \pm .93	25.1 \pm .67	2.7 \pm .92	9.8 \pm 1.15
Phosphate	1	14.4 \pm .24	15.5 \pm .33	10.7 \pm .23	3.7 \pm .33	4.8 \pm .41
	2	11.3 \pm .20	10.7 \pm .28	7.4 \pm .20	3.9 \pm .28	3.3 \pm .35
	3	13.3 \pm .27	13.9 \pm .32	10.3 \pm .20	3.0 \pm .33	3.6 \pm .38
pH	1	5.51 \pm .032	5.73 \pm .034	5.72 \pm .043	-.21 \pm .054	.014 \pm .033
	2	6.34 \pm .059	6.15 \pm .056	5.94 \pm .056	.40 \pm .081	.021 \pm .079
	3	6.30 \pm .048	6.09 \pm .050	6.15 \pm .056	.15 \pm .074	-.063 \pm .075
Organic acid	1	12.64 \pm .26	17.50 \pm .48	11.74 \pm .31	.9 \pm .40	5.76 \pm .57
	2	14.44 \pm .41	18.96 \pm .60	13.71 \pm .46	.73 \pm .62	5.25 \pm .75
	3	13.60 \pm .34	19.39 \pm .53	13.66 \pm .43	.06 \pm .55	5.73 \pm .68

The first specimen (1) is passed on rising, the second (2) after breakfast, and the third (3) on going to bed. For further details as to methods of collection and analysis the previous paper¹ should be consulted.

It will be seen that the differences while present are not great. In the first morning specimen the free and total acid values are similar to the 'Great Ormond Street' values and show a definite difference from the control, but during the day the values approximate to the normal group. The increased phosphate output is again present to an almost similar degree. The difference in the organic acid values from the normal seen in the 'G.O.S.' series is not repeated, the Carshalton values being identical with the control group. On the other hand the pH which showed no difference in the 'G.O.S.' series from the normal, shows a barely significant increase

in acidity in the first specimen, and a definitely significant increase in alkaline tide in the second specimen.

The following conclusions may be drawn:—(1) The first morning specimen reflects underlying diathesis, less influenced by diet. (2) The subsequent specimens are influenced to a great extent by diet. (3) There is an excess acid production in children suffering from rheumatism. (4) The excess of organic acid is largely of dietetic origin.

This increased output of acid may be due either to an inborn variation in the acid metabolism (the 'acid diathesis') or to the effect of the rheumatic infection itself.

A subdivision of the Carshalton cases was made by Dr. Gray Hill into three groups (1) 'rheumatic heart disease,' (2) 'chorea' and (3) 'subacute rheumatism.' It was thought probable that the intensity of the rheumatic infection itself would be different in these three groups. The following table shows the results.

TABLE 2.

ESTIMATION	SPECIMEN	RHEUMATIC GROUPS.			TOTAL GROUP
		1	2	3	
Free acid	1	17.08 ± .84	18.12 ± .74	17.2 ± .54	16.9 ± .35
	2	10.2 ± .92	8.5 ± 1.12	7.3 ± .78	8.6 ± .43
	3	10.11 ± .87	10.75 ± 1.03	10.77 ± .78	9.99 ± .39
pH	1	5.56 ± .08	5.53 ± .08	5.47 ± .04	5.51 ± .032
	2	6.21 ± .12	6.27 ± .16	6.22 ± .12	6.34 ± .059
	3	6.35 ± .11	6.51 ± .11	6.28 ± .09	6.3 ± .048
Organic acid	1	13.48 ± .70	13.31 ± .64	12.63 ± .42	12.64 ± .26
	2	14.9 ± 1.06	14.5 ± 1.13	15.12 ± .92	14.44 ± .41
	3	13.76 ± .94	14.5 ± 1.10	13.46 ± .68	13.60 ± .34

It will be seen that no sub-group differs from the main group by a significant amount. It may be concluded from this that there is an 'acid diathesis' in acute rheumatism in children.

Summary.

A further group of children under conditions more nearly similar to those of the control group of the previous communications has been examined with respect to their acid output. This group has been further

divided into sub-groups of different types of infection. It is concluded that the morning specimen of urine is less influenced by diet and shows the existence of an 'acid diathesis.'

Thanks are due to Sir Frederick Menzies and Dr. Pugh for permission to carry out this investigation at the Queen Mary's Hospital, and to Dr. Gray Hill for pointing out the possibilities of this group of children and for the continued interest and trouble he has taken in selecting and grouping the children. This work would not have been possible without his help.

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AMYOPLASIA CONGENITA ASSOCIATED WITH MONGOLISM

BY

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The rare condition known variously as multiple congenital articular rigidity, arthrogryposis multiplex congenita and amyoplasia congenita has been made known in this country mainly by the work of W. Sheldon², who introduced the name used in this paper. A further title has been applied by D. S. Middleton¹, who uses the term myodystrophia foetalis deformans, as being more accurately descriptive of its probable pathogenesis. The present case is particularly interesting on account of its association with mongolism and because of certain similarities between the two conditions. The presence of deformities of the bones in the affected joints is also noteworthy.

Case report.

The patient, a girl, aged seven-and-a-half years, was admitted to the Fountain Hospital for mental defectives on November 8, 1933.

Family history. The parents are unrelated and were both twenty-nine years old when the patient was born. The father, a mechanic, is stated to be normally intelligent and in good health. The mother is of fair education and intelligence, but 'highly-strung.' The patient was the last of three pregnancies; the first child, now a boy of fourteen years, is said to be normal in every way and to be doing well at school, and the second was a three months' miscarriage. No abnormalities or further points of interest in the family history can be discovered.

Gestation and birth. Except for 'some haemorrhage after a long omnibus ride which passed off after a night's rest' in the third month of pregnancy, the mother enjoyed good health until the sixth month, when she suffered from a considerable amount of vomiting, especially at night. She experienced no severe shocks, falls or accidents of any kind nor had she been irradiated by x-rays or radium. The child was born at full term and delivery was rapid (first stage—3 hours; second stage—10 minutes; third stage—5 minutes). Birth occurred in an unreduced right occipito-posterior position with extended legs, the face and brow presenting themselves first. The amount of amniotic fluid was normal and there was no premature rupture of the membranes. The placenta was cyanotic in appearance. Birth weight was 6 lb. (I am indebted to the British Hospital for Mothers and Babies, Woolwich, for this information as regards labour). The mother reports that the baby's weight soon went down to 3 lb. and that she was so flaccid that her head 'flopped back to touch the middle of her back.' Her legs were deformed from birth and appeared to be 'back to front.'

Early childhood. At the age of eight weeks she attended the Royal National Orthopaedic Hospital, and to the authorities there my thanks are due for the following information. She was found to be suffering from congenital genu recurvatum, severe bilateral congenital equino-varus and cervical opisthotonus. Her musculature was very poor. She was treated by stretching and splinting and later by tenotomy of the tibiales tendons. At the age of two years she was admitted to the Hospital's country branch, where daily manipulations, stretching and treatment by means of the mercury vapour lamp effected some improvement. Whilst there she suffered from paroxysmal tachycardia.

State on admission. She was a fairly well-nourished girl of seven-and-a-half years, suffering from a severe degree of mental deficiency and a remarkable deformity of the lower limbs. She was considerably below average height and weight and showed many mongol characteristics, her general appearance, skin, hands, palate, ears, epicanthus, flabbiness and hypotonia and especially her articulation, mannerisms and general personality being typical of this condition.

Physical characters. Her head circumference was nineteen-and-three-quarter inches (50 cm.) and her cephalic index 71, denoting a rather more dolicocephalic configuration than is usually associated with mongols. Another trait uncommon in mongolism was shown in her possession of curly hair. Her eyes appeared to be widely separated and the palpebral fissures small, because of a well-marked bilateral epicanthus. The space between the eyes was 36 mm. Pupil reactions, vision and fundi were normal. The ears were small and lobeless. The hard palate was high and narrow-arched, with a long overhanging soft palate; the tonsils were large and unhealthy; the buccal mucous membrane was hyperaemic and always liable to inflammation and ulceration and the gums were spongy. Her hands were short and podgy and her skin scaly and dry.

Speech was monosyllabic, explosive, very indistinct and typically mongol in character. Her words were usually accompanied by simple gestures and she made no attempt to string together even elementary phrases. Lalling was exhibited in her substitution of T for hard C or K. Her contours were rounded owing to subcutaneous fat, but her muscles were flabby and toneless and her ligaments very lax. Abnormal mobility was present at all joints except the knees and ankles, where deformity was present. The extreme range of movement at the hip joint can be seen in fig. 1 and her ability to entwine neighbouring toes was remarkable.

Cardiovascular system. No obvious heart lesion was present, but her peripheral circulation was poor and she was subject to frequent chilblains. This picture of peripheral stagnation is, of course, not confined to mongols, but outside mongolism it is mainly found in anergic aments of low grade.

Central nervous system. Knee and ankle jerks were impossible to obtain owing to her deformities. Tendon reflexes were sluggish, but equal. Plantar reflexes were flexor and abdominals present and equal.

Other systems were normal. Serum Wassermann and Meinicke macro-klarung reactions were negative.

Deformities. There was a bilaterally symmetrical genu recurvatum of such a degree that the knees appeared to be facing backwards (fig. 2). The legs were usually held in a position of hyperextension, and flexion beyond 180 degrees either by active or passive movement was impossible. The whole range of movement at the knee joint was approximately thirty degrees.



FIG. 1.—General appearance. Note hyper-mobility at hip-joint.



FIG. 2.—Walking position.

The patellae were not palpable. The feet were fixed in an extreme varus position with some degree of equinus (fig. 3). Practically no movement could be elicited at the ankle joints.

Gait. She was unable to walk or even assume an upright posture, but was able to get about very actively on all fours, progressing in a typically simian manner. Her weight was borne mainly on her palms and on the dorsal surfaces of her feet, her legs being hyperextended and her buttocks sticking out prominently in a backward and upward direction (fig. 2). She was wont to end her journeys with a rapid turn into a sitting position and an exceptionally beaming smile.

X-ray examination. Skiagrams showed no bony abnormalities except in the region of the knee joint. Here gross deformity and posterior subluxation of the lower end of the femur was apparent. The patellae could be faintly seen well above their usual site and were obviously undeveloped (fig. 4). The hip joints showed no sign of dislocation. Dr. Peter Kerley was kind enough to examine the films and reported that the structure of the bones and epiphyses was normal and that there was no sign of developmental or acquired lesion. The muscles showed no radiological abnormalities. Soft x-rays were not taken.

Mental state. INTELLIGENCE. Her mental age was approximately two years. She could point to her nose and was able to pick out, but not name, common objects, such as a penny, key, pencil or scissors. She could obey simple orders, but was unable to execute two consecutive commissions. She failed to give her name or sex, but was able to recognize a paper-wrapped sweet and would undo it before putting it into her mouth. Her attention was difficult to hold and she did not try to co-operate in any way. She was unable to use a spoon and made no effort to help in dressing or undressing herself. Her habits were faulty and she required every personal attention.

BEHAVIOUR. She was a lively and mischievous child, inclined to be aimlessly destructive with toys and other objects. The simplest kind of constructive playing was quite beyond her powers. Her nature was cheerful and contented and she seldom cried. She liked plenty of attention and appeared to take considerable pleasure and pride in strutting round in front of other children or visitors. Her smile, her mannerisms and her whole nature were typical of the mongol.

Progress. She soon settled down happily, showing interest in her surroundings and neighbours and becoming a general favourite. Her physical condition, like her character and conduct, conformed to mongol expectations and she soon showed herself to be delicate and to have little resistance against infection. In January, 1934, she suffered from cellulitis of the right leg and thigh, in February from Vincent's angina, which cleared up rapidly after two arsenical injections, and in March from a feverish cold and cough. During June she became much more subdued and lacking in energy. No physical signs to account for this were present, but she went off her food and was obviously unwell. She recovered, however, and was quite at her best until she contracted scarlet fever in September. On January 7, 1935, she was put to bed with an ordinary afebrile cough and cold. No physical signs developed, but, as in June, she was very listless and 'floppy.' Three days later she died suddenly, shortly after sitting up in bed quite happily and comfortably.

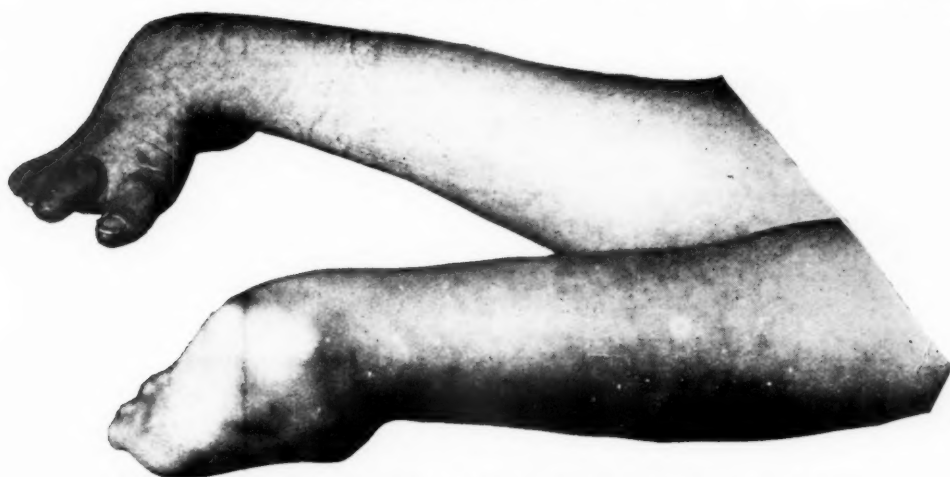


FIG. 3.—Showing the deformity of the feet. Note wide space between first and second toes.



FIG. 4.—X-ray of knee-joint.

Pathological examination. A substantial layer of subcutaneous fat was present, but the muscles were pale and exiguous. The heart was exceptionally large and heavy, weighing 184 gm. There was general muscular hypertrophy, but no dilatation. The right side was filled with dark coloured clot. There were no congenital anomalies. The liver was pale and greasy and weighed 539 gm. Sections showed a state of extreme fatty degeneration with moderate venous engorgement. The nuclei were well preserved, but the cytoplasm was almost entirely replaced by fat, especially in the neighbourhood of the hepatic veins. The thyroid approximated to the foetal type. The acini were small and the colloid scanty. There was proliferation both of the epithelial cells and of the inter-acinous fibrous tissue. The brain weighed 1,134 gm. and, as the shape of the skull suggested, was not as rounded as is usual in mongolism. A small tumour about the size of a large pea was found attached to the wall of the right lateral ventricle. Sections showed it to consist of choroid plexus tissue. The lungs, kidneys, spleen, pancreas, suprarenals, ovaries, thymus and pituitary body showed no naked-eye or microscopical abnormalities.

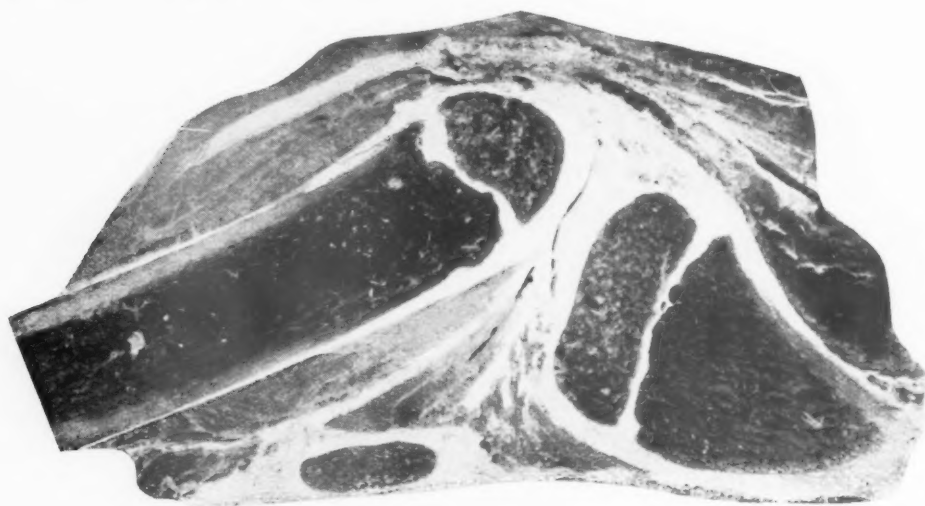


FIG. 5.—Knee-joint.

KNEE JOINT (fig. 5). The tibia was subluxated forwards on the femur, apparently owing to the anterior part of the femoral condyle having failed to develop. Not more than 30° of movement was possible and the joint became locked at 180° . The existence of the semilunar cartilages and of the cruciate ligaments could not be definitely determined. If the latter were present, they must have been greatly stretched out. The muscle tissue, normally to be found around the joint, was for the most part replaced by fibrous tissue and fat, embedded in which were areas of calcification. Apart from this the muscle was of normal appearance.

Discussion.

The present case differs from other published cases of amyoplasia congenita in several ways. In the first place normal intelligence has been definitely recorded in the majority of cases and mental deficiency has only once been noted (Middleton). Secondly, the distribution and position of the deformities do not fall in with any of Rocher's three main clinical

types⁵, although these types are by no means all embracing. Of greater interest is the occurrence of actual hyper-extension at the knees with complete flexion-inability beyond 180°. Although extension deformity at the knee joints, usually in combination with abnormalities of other joints, has been commonly described in this condition (Rocher^{5, 6}, Rocher and Ouray⁷, Sheldon⁹, Middleton¹, Schapira⁸), no record of the deformity reaching such a degree of genu recurvatum has been discovered by the writer. Thirdly, x-ray examination has shown in most cases that a normal bony disposition is a feature of the affected joints. The presence of osseous deformity as seen at the lower end of the femur in this case is exceptional. There can be no doubt that this deformity, as well as that of other joint elements, is secondary to the muscle defect and the fact that bony changes occur so seldom suggests that the condition does not arise until late in foetal life.

There can be no doubt that the present case was one of mongolism, despite some minor discrepancies, such as the shape of the head and the curly hair. Mongolism is remarkable for the large number of its physical signs and for the fact that no one of them is invariably present. Despite this there is usually sufficient evidence, as in this case, to make the picture unmistakable.

The maternal and pre-natal history shows no evidence of early amniotic infection, a possibility suggested by Price, unless the previous miscarriage be considered as suggestive of low-grade uterine infection.

Diagnosis.

The diagnosis of amyoplasia congenita cannot be considered as certain in this case, but several factors point very strongly to this condition. The main features of amyoplasia congenita may be said to be:—

- (1) Congenital joint rigidities of varying degree, usually symmetrical and always without inflammatory change.
- (2) Hypoplasia or degeneration of those muscles which normally produce the movements which the child is unable to perform.
- (3) Absence of any hypertonia or hypertrophy of antagonistic muscles, showing that the immobility is not attributable to muscular overaction.
- (4) Sudden checking of movement at the affected joints, which no application of force can increase, pointing to bony or fibrous changes of the joint structures. The fact that mobility is not increased under general anaesthesia corroborates the last two points.
- (5) Weak or absent faradic responses in affected muscles, but no reaction of degeneration.
- (6) No sensory or trophic changes.
- (7) Normal intelligence.
- (8) Extensive fibro-fatty changes in the affected muscles.

The present case illustrated the characteristic type of joint rigidity, sudden checking of movement, and absence of hypertonia and sensory or trophic change. Electrical reaction tests were unfortunately not available at the hospital and the child was physically unfit to travel. Only one

previous case appears to have suffered from mental defect, but in the present case this was but a part of the syndrome of mongolism, the association of which with amyoplasia congenita must now be considered. The characteristic fibro-fatty changes were found in the muscle tissue in the neighbourhood of the knee-joint.

Mongolism and amyoplasia congenita.

There would appear to be no obvious association between mongolism, which is probably caused by some defect of maternal or foetal metabolism in the early weeks of intra-uterine life, and amyoplasia congenita, which appears to be due to a more or less localized muscular maldevelopment; and it may be said at once that etiological connection is unlikely. There are, however, individual points of similarity. The pseudo-oedematous appearance, due to a generalized subcutaneous fatty deposit is common to both conditions. Sections show this deposit to be true fat. The musculature shows a certain superficial similarity, but microscopy reveals a very different picture. No gross abnormalities are found in mongol muscle, whereas the affected muscles in amyoplasia congenita show only a few healthy muscle fibres, the remainder being replaced by fat and fibrous tissue. It is worthy of mention that neither syndrome shows any hereditary or familial tendency, although a definitely hereditary condition occurs in lambs (Roberts^{3,4}), which is clinically and pathologically akin to amyoplasia congenita. The age of the mother and other etiological factors significant in mongolism have yet to be ascertained in cases of amyoplasia congenita. Lastly the facial resemblance between the present case and Fairbank's third case⁵ is not without interest.

In the present case only the characteristic deformity of the knee joints and to a lesser degree of the ankles was peculiar to amyoplasia congenita. The condition of the muscles, except in the immediate neighbourhood of the knee joints, could equally well be attributed to mongolism. On the other hand, the local picture is so typical of amyoplasia congenita that this diagnosis cannot be reasonably withheld.

Pathogenesis.

The various theories of the causation of this condition have been reviewed and discussed by Sheldon, who maintains that the joint-structure deformities are secondary to the muscle changes and that the primary defect is in the nature of a developmental aplasia or hypoplasia of certain muscle groups. More recently Middleton¹ has described atrophic changes in the affected muscles more suggestive of a degeneration in the later stages of intra-uterine life than an actual hypoplasia. The changes resembled those seen in some cases of muscular dystrophy and Middleton believes amyoplasia congenita (myodystrophia foetalis deformans) to be a pre-natal form of myodystrophy. It is true that his evidence is drawn from a single case, which was complicated by what appeared to be an upper motor neurone

lesion, but he has also described a similar, though more active process of muscle degeneration in the closely related condition of congenital 'stiff jointed lambs,' described by Fraser Roberts^{3,4}. This condition differs from the one under discussion in that it is definitely hereditary and has been proved to be due to a simple autosomal recessive factor.

In other cases of amyoplasia congenita there has been found a simple replacement of muscle by fat and fibrous tissue, mainly the former, and when muscle fibres remain, they are of normal appearance. When a somatic structure fails to develop or when it has completely atrophied, it is usual for fat to take its place, so that the fatty changes seen in the affected muscles do not favour the one theory more than the other. The evidence in favour of Middleton's myodystrophic theory rests almost entirely upon the finding of actually degenerating as opposed to hypoplastic muscle tissue in one case. The absence of degenerative changes in other examined cases may, however, be due to the atrophic process having been completed, and therefore invisible, at the time of histological examination. If muscle sections could be examined in the later stages of intra-uterine life, as was done in that case of Roberts's lamb disease which showed actively degenerating muscle, a similar picture of atrophic process might well come to light.

The possibility of a nervous origin has been suggested by the case, originally published by Dorothy Price², in which Middleton found atrophic changes. In this case atrophy of certain muscle groups and limitation of joint movements were associated with a generalized spasticity, with adduction spasm of the legs, in fact, a congenital spastic diplegia. The pathological findings of a diffuse chronic meningo-myelitis and mild hydrocephaly support this conclusion and the fact that 'the anterior horn cells appeared to be normal in size and number' is directly antagonistic to a neuronie conception of the origin of the muscle defect. In uncomplicated amyoplasia congenita there is no spasticity and no hypertonia of antagonistic or other muscles, the limitation of movement being entirely mechanical and not due to muscular spasm.

It would appear that both Price's and the present case are true examples of amyoplasia congenita, the former complicated by congenital spastic diplegia and the latter by mongolism. There is at present no valid evidence that amyoplasia congenita is due to a lesion of nervous structure, all available histological findings pointing to the muscle as the primary pathogenic site. It has not, however, been definitely established whether the lesion is hypoplastic or, as seems more probable, atrophic.

I have pleasure in acknowledging my indebtedness to Dr. W. Sheldon for much helpful advice, to Dr. R. J. V. Pulvertaft for histological reports and to Mr. E. P. Brockman for examining the knee joint. I would also thank Dr. James Nicholl, medical superintendent of the Fountain Hospital, for permission to publish the case and Mr. J. E. Stevens for the photographs.

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NOTICE TO CONTRIBUTORS.

It is proposed to publish from time to time reports of single cases which are of special interest and importance.

CASE REPORT

CONGENITAL OBLITERATION OF THE BILE DUCTS*

BY

REGINALD WILSON, B.A., M.D., D.C.H.

John Thomson¹ has shown that the clinical condition entitled congenital obliteration of the bile ducts may depend upon a number of somewhat different anatomical deformities. From his study he concluded that the pathological process was primarily a developmental arrest. He described aplasia and narrowing of the ducts which he believed caused obstruction. This he thought gave rise to the cirrhosis of the liver which is so constantly found at autopsy. Opposing this view Rolleston^{2,3} later suggested that there was a placental toxæmia which had its effect upon the foetal liver causing a cholangitis. This was a descending process which resulted in an inflammatory thickening of the duct walls, and thus a stenosis.

Case record.

A. E., a female child, was six months of age when admitted to the Westminster Hospital. The complaints were jaundice, boils on the buttocks, and failure to gain weight. The jaundice had had its onset very insidiously in the first weeks of life. The infection was a more recent affair. The parents are both well and their Wassermanns are negative. They have four other children, three of these were slightly jaundiced during the neonatal period, but in none did it persist.

EXAMINATION revealed an emaciated yellow child, with an enlarged liver and spleen. There were staphylococcal abscesses of the buttocks. The stool was usually almost white, but was occasionally streaked with bile. This was shown not to be urinary contamination, although the urine did contain large amounts of bile. The blood Wassermann was negative.

PROGRESS. The infection gradually subsided, but the degree of jaundice did not alter, and the child never gained weight during the subsequent eight weeks in Hospital. Measles and a complicating bronchopneumonia finally caused death.

PATHOLOGICAL FINDINGS. The skin, sclerae and all organs were deeply bile-stained. There were numerous healed scars on the buttocks. The lungs showed bronchopneumonia. The liver was firm and its dark green surface had a granular appearance. Bile could not be squeezed from

* The study of this case was undertaken during the tenure of the Wander Research Scholarship at the Westminster Hospital and I am indebted to Dr. Reginald Lightwood for special facilities for investigation supported by the Thomas Smythe Hughes Medical research fund,

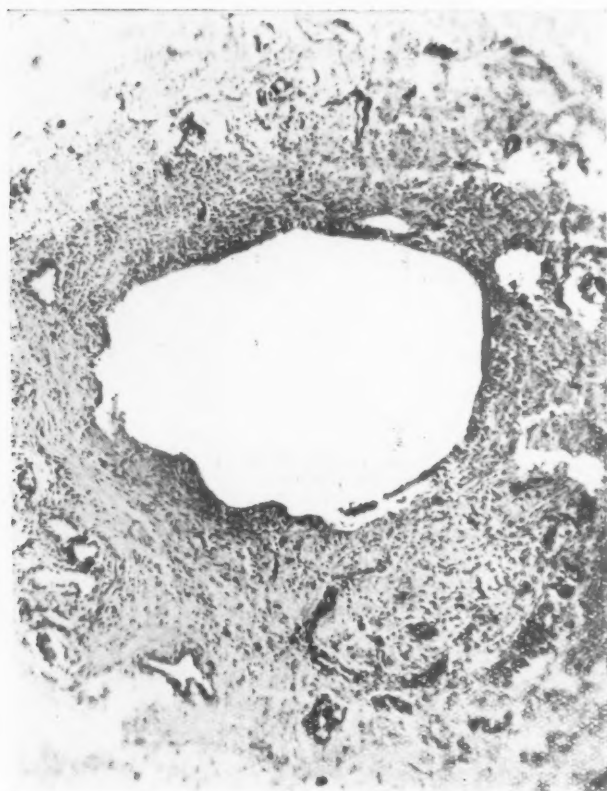


FIG. 1.—Common bile duct to show thick wall and narrow lumen.

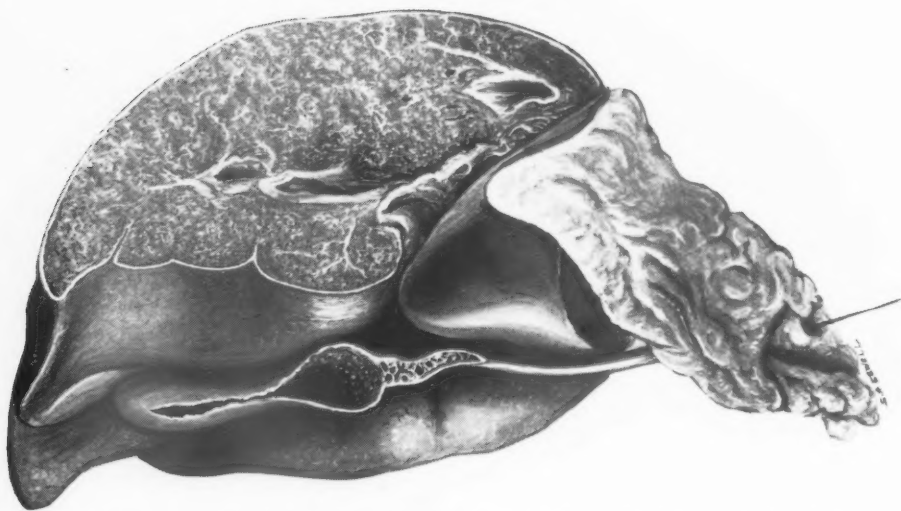


FIG. 2.—Drawing of the liver with dissected cystic duct showing its vacuolated condition.

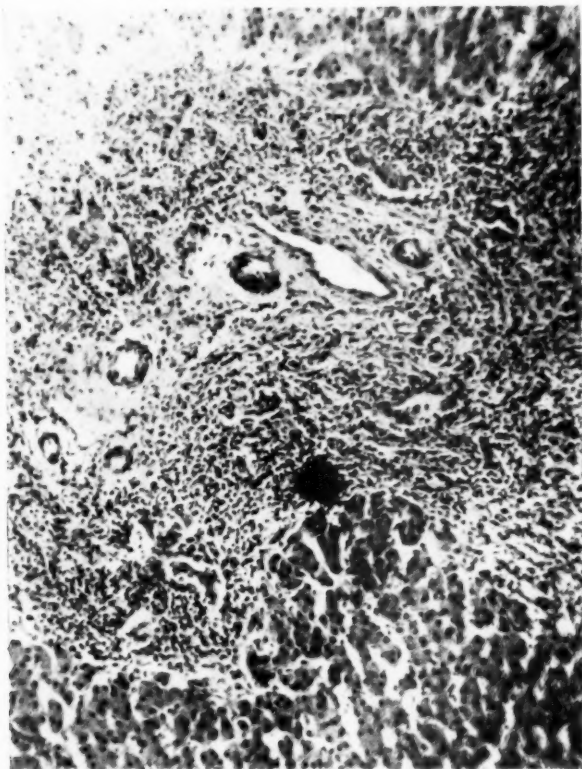


FIG. 3.—Microphotograph of the liver showing coarse fibrosis of the portal tract and small atrophic bile ducts.



FIG. 4.—Wall of the cystic duct showing its thickness and honeycombing.

the ampulla of Vater when pressure was exerted on the small gall bladder. A firm bristle could, with difficulty, be passed from the ampulla along the common duct into the hepatic duct; the walls of both of these were very thick (fig. 1).

On opening the gall bladder it was found to be thickened, and to contain a little greenish mucus. The first part of the cystic duct was carefully opened by cutting away the superior surface. No opening from the gall bladder could be discovered, and the thick-walled duct had its lumen honey-combed with bands of tissue (see fig. 2). No continuous lumen could be found till the lower third of the duct was reached. For the sake of comparison the bile duct system of a new-born infant, who had died of an injury, was dissected. The spiral valves of Heister were demonstrated and the cystic duct could be probed with ease.

MICROSCOPIC EXAMINATION of the liver showed a widespread fibrosis, irregularly arranged but chiefly affecting Glisson's capsule (fig. 3). The bile ducts were small and atrophic, and surrounding them were aggregations of small round cells. There was much bile staining. Sections through the cystic duct showed it to be devoid of the normal columnar epithelium. The muscle coat was atrophic and the lining epithelium was composed of flattened polyhedral cells two to four cells deep. There appeared to be one main lumen, but the walls showed smaller spaces, the lining of which was similar to the main lumen (fig. 4). There were no glands in the wall, and the signs of inflammation were lacking.

Discussion.

Keith⁴ states that the common bile duct, the gall bladder and the cystic duct are developed from the hind part of the hepatic diverticulum of the fore gut. The hepatic ducts arise from the solid liver outgrowth. The lumen of the gall bladder and ducts is occluded by an epithelial proliferation during the second month. In normal development this condition becomes vacuolated, the vacuoles coalesce and the lumen becomes established.

Such an arrest in the vacuolated stage would account for the situation in this case. Careful comparison of the gross and microscopic anatomy between this and the normal case emphasized the pathological significance of the vacuolated condition of the cystic duct, which may represent an arrest in the process of canalization.

Summary.

A case is presented in which:—

1. The gross and microscopic anatomical findings suggest that jaundice was due to a partial stenosis of the common bile duct. The cystic duct shows evidence of arrest at an early stage of foetal development.
2. An unusually long period—eight months—ensued before death from intercurrent infection took place.

I wish to thank Dr. Donald Paterson for permission to publish this case.

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CONGENITAL TRICUSPID ATRESIA

BY

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Congenital tricuspid atresia is an infrequent malformation of the heart. Abbott¹ in her analysis of 1,000 congenital cardiac cases gives sixteen examples. To these may be added the cases of Bellet and Steward², Murphy and Bleyer³, and Grayzel and Tennant⁴, making a total of nineteen cases in the available literature. It is probable, however, that many cases escape recognition from lack of a post-mortem examination, or from the assumption that the cyanosis invariably present is the result of some obstructive lesion of the pulmonary tract. In the case here recorded laboratory examination enabled the exclusion of a stenotic pulmonary lesion, but the diagnosis was not certain until autopsy. Two main types of tricuspid atresia are described. Isolated tricuspid atresia, with which are associated interauricular and interventricular septal defects and other secondary changes is the commoner type. The other group comprises those cases in which the tricuspid atresia is associated with transposition of the vessels or other abnormality. Duration of life is longest in this second group. This communication is concerned with isolated tricuspid atresia.

Case record.

A male child came under observation at the age of five months on account of cyanosis dating from birth. He was poorly developed and weighed 5 lb., and had failed to gain weight. He was dyspnoeic at rest. Marked cyanosis was present, and the least movement or such simple acts as feeding or crying led to increased cyanosis and respiratory distress. There was no clubbing of the fingers or toes.

On examination there was evident enlargement of the heart, the apex beat being forcible in the anterior axillary line. A mesocardial systolic thrill of variable intensity was present. A systolic murmur, rough in quality, was heard over the precordium and was loudest over the base of the heart. It was heard widely over the back but not in the neck. The liver was palpable but the spleen was not enlarged.

X-ray examination (fig. 1) showed a globular heart with exaggerated convexity of the right and left borders suggesting right auricular and left ventricular hypertrophy.

The electrocardiogram (fig. 2) showed marked left axis deviation. The P wave in lead II was large and the T wave in lead I diphasic.

Death from bronchopneumonia occurred at the age of eight months.

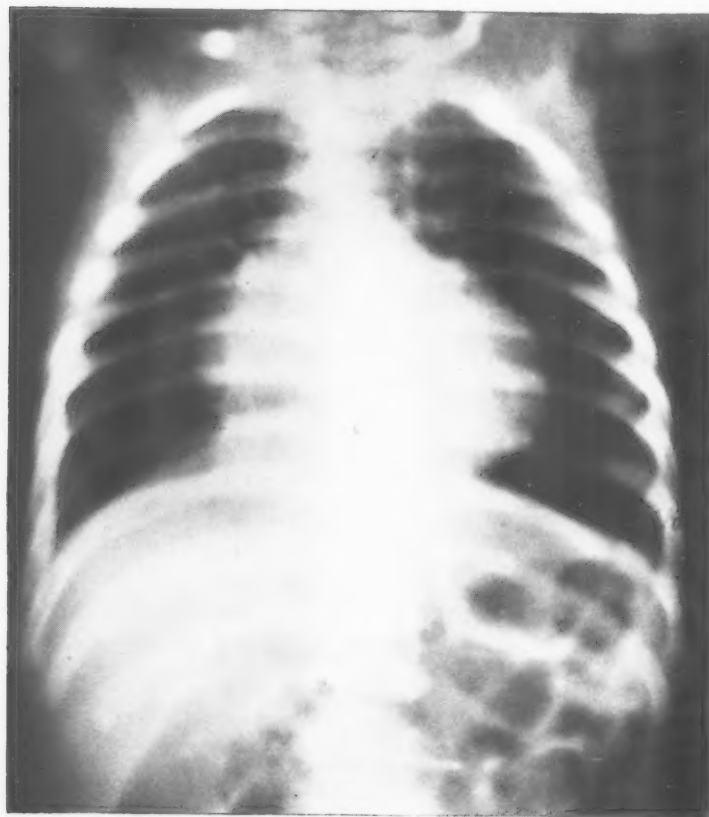


FIG. 1.—X-ray appearance of heart.

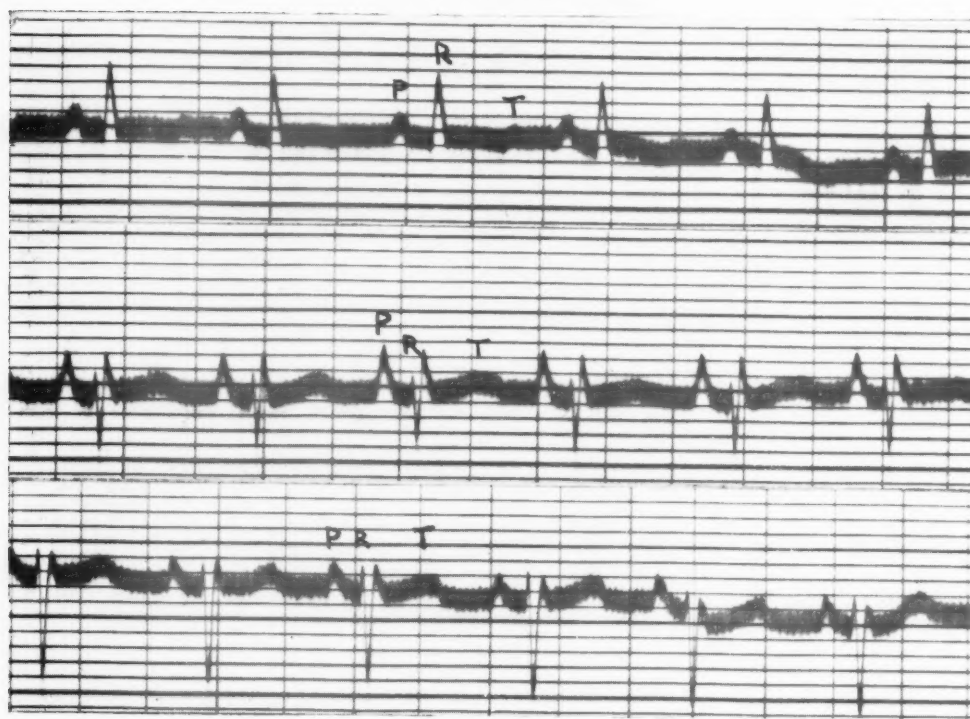


FIG. 2.

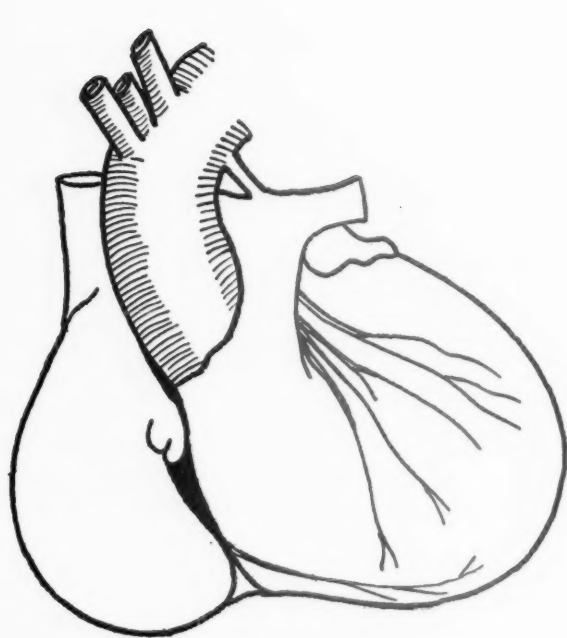
POST-MORTEM EXAMINATION. The heart was greatly enlarged and globular in shape (see fig. 3). The anterior surface of the heart consisted mainly of the left ventricle and the dilated right auricle. The aorta appeared to be much larger than normal and arose in its normal relationship to the pulmonary artery. The left ventricle was dilated and hypertrophied with walls 10 mm. thick. There was an oval shaped defect of the upper part of the interventricular septum (fig. 3 B and C), anterior to the membranous septum and beneath the non-coronary cusp, from which latter it was separated by a band of fibrous tissue. The defect measured 5 by 4 mm. The sinus of the right ventricle was small and rudimentary, and of about the capacity of a hazel nut. There was no evidence of tricuspid leaflets or papillary muscles. The conus of the right ventricle was narrow with thick walls. The defect of the interventricular septum opened beneath the crista supraventricularis. The pulmonary artery was of normal calibre and the pulmonary cusps were normal. The right auricle was dilated and hypertrophied. There was no tricuspid orifice and its normal site was marked by an elliptical depression (fig. 3 D). Relatively thick muscular tissue intervened between the right auricle and ventricle. A large patency of the foramen ovale admitted the little finger. The left auricle was moderately dilated but its walls were not hypertrophied. The mitral valve was normal. The aorta was enlarged relative to the pulmonary artery but its walls were healthy. The aortic cusps, three in number, presented no abnormality. The ductus arteriosus was closed.

An accessory spleen was present.

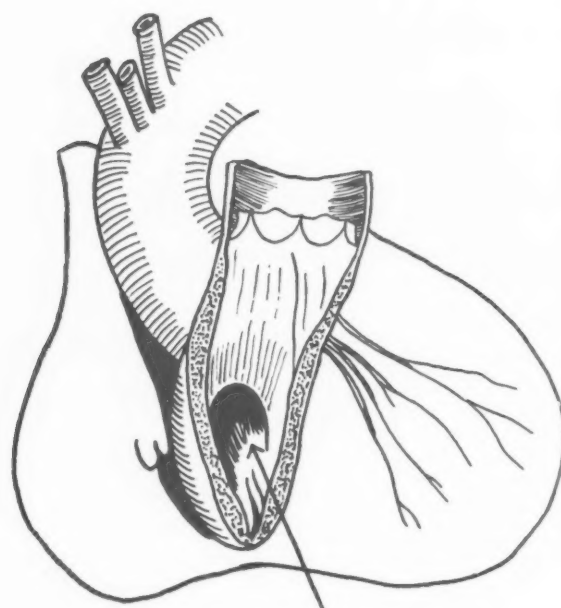
ANATOMICAL SUMMARY. Atresia of the tricuspid orifice; interauricular septal defect; interventricular septal defect; hypertrophy and dilatation of the right auricle and left ventricle; rudimentary cavity of the right ventricle.

Discussion.

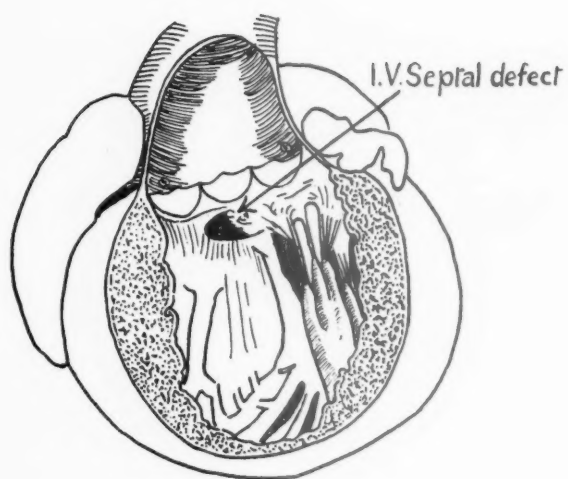
Such a combination of defects as are present in this case are the constant findings in isolated tricuspid atresia. The primary lesion is atresia of the tricuspid orifice which may be so complete that not even a scar indicates the site of the opening. More frequently a slight depression or a few muscular bands, as in the present case, are found to mark its normal site. The right ventricle is always extremely small and aplastic, in size scarcely the volume of a nut (Laubry and Pezzi⁵), or existing as a small irregular flattened space in the wall of the right ventricle, which might well be overlooked (Robertson⁶). Some cases, as for example that of Robertson, have been described as a type of cor biatriatum triloculare. The right auricle is dilated and hypertrophied. There is always an interauricular septal defect, either a widely patent foramen ovale or other abnormality of the septum. There is nearly always a defect of the interventricular septum (87.5 per cent. Abbott's series) and this may open, as in the present case beneath the crista, or directly into the conus of the pulmonary artery. The ductus arteriosus was patent in only 37.5 per cent. of Abbott's cases. In the absence of a patent ductus, which would assure a limited supply of blood to the pulmonary circulation, it is evident that the defect of the interventricular septum is essential for the maintenance of the circulation. The increased work performed by the left ventricle leads to its hypertrophy.



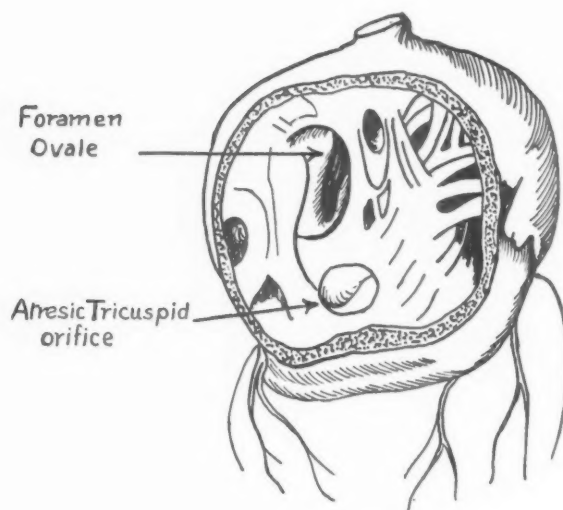
(A) External view of heart.

*I.V. Septal defect*

(B) Right ventricle opened.



(C) Left ventricle opened.



(D) Right auricle.

FIG. 3.

Various theories have been advanced in explanation of the abnormality. Unequal division of the common auriculoventricular orifice by the abnormal growth of the anterior and posterior endocardial cushions, so that these adhere to the right wall of the common orifice, would appear to be the most satisfactory theory. Such an idea has been embodied by Abbott in her statement that the abnormality 'arises as the result of malposition and irregular union of those parts of the cardiac septa dividing the mitral from the tricuspid ostium.' Obliteration of the tricuspid orifice takes place at about the fourth week of foetal life and closure of the septa occurs at the eighth week. It is probable that raised pressure in the left ventricle is an important factor in maintaining a conduit between the two sides of the heart.

No case of tricuspid atresia has so far been diagnosed during life. As some of the cases survive until late childhood, or even to puberty or later, the clinical features are worthy of consideration. The presenting symptoms are cyanosis of marked degree, and clubbing in cases that survive more than a year. Cyanosis exists from birth and is enhanced by movement or emotion. The heart is enlarged to both left and right sides and the apex beat is forcible. Laubry and Pezzi insist on the value of percussion of the back as a means of detecting enlargement to the right of the vertebral column in children. A mesocardial systolic murmur is commonly present, and may be heard widely over the chest. A systolic thrill is present in 12.5 per cent. of cases (Abbott). X-ray examination shows an enlarged and globular heart. The convexity of the right border, corresponding to the right auricle, is exaggerated. The left border is well rounded and presents the appearance of left ventricular hypertrophy. The gross enlargement of the right auricle and the slight enlargement of the left can be confirmed in the oblique positions. The electrocardiogram shows normal or left axis deviation. The P wave may be enlarged or notched suggesting auricular hypertrophy.

The dictum of Fallot that 74 per cent. of cyanotic cases were examples of his tetralogy has perhaps led to the assumption by the physician that any congenital cyanotic case surviving more than a few days must almost always be the result of a stenotic pulmonary lesion with associated septal defect permitting a shunt. Apart from the interest that a cyanotic case evokes, little effort has been made until recently to identify anatomical lesions in this group. The advent of laboratory aids in the investigation of cardiac disease has at any rate enabled the segregation of those cases in which there is a stenotic lesion of the pulmonary tract and septal defect from the smaller group of cases where some other abnormality causing cyanosis exists. The skiagram is distinctive in some conditions, notably the tetralogy of Fallot, and the auricular septal defect. In tricuspid atresia the enormous right auricle and the hypertrophied left ventricle are suggestive. Of more importance is the electrocardiogram. The finding of normal,

and particularly of left axis deviation in a cyanotic case should at once exclude the tetralogy or any lesion of the pulmonary tract. Pulmonary stenosis with a closed septum, which may rarely be associated with normal axis deviation, is not accompanied by cyanosis except as a late or terminal event. The tetralogy of Fallot is always accompanied by right axis deviation unless dextrocardia or gross conduction defect are present.

Summary.

A case of isolated tricuspid atresia has been presented and its main features discussed. It is suggested that this abnormality might be more frequently diagnosed if the radiological and electrocardiographic pictures were carefully considered.

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ACCESSORY NASAL SINUSITIS IN CHILDHOOD

BY

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WITH A RECORD OF BACTERIOLOGICAL EXAMINATIONS

MADE BY

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Introduction.

Disease of the para-nasal sinuses in childhood has received little recognition in this country. There are some half dozen papers extant upon the subject, notably those by Cleminson¹ and Mollison², together with a small number of case reports. Such literature as there is does not appear to have received the attention it merits from those practising among children. On the other hand, American writing upon the subject is profuse, and makes it clear that nasal accessory sinus suppuration vies with disease of the tonsils and adenoids as a diagnosis in the upper respiratory infections of the children in the United States. Referring to the American writers in his classical work entitled 'Nasal Accessory Sinusitis' Hajek says:

'I have seen a great many children between the ages of seven and twelve with complicated sinus infections. The fantastic reports of some American authors (Dean, Ele, and La Mere) who describe an enormous number of empyemas observed in the earliest years of childhood (Dean speaks of 100 cases), are to be regarded with great scepticism, as their methods of examination give us no assurance of the reliability of their results.'

In this paper the average age of a series of a hundred cases is seven-and-a-half years; the total number of children under seven years is forty-two; the youngest is two-and-a-half, and the oldest twelve. Thus there are obviously great differences of opinion upon the frequency and importance of infections of the para-nasal sinuses in childhood. In view of the prevalence of infections of the ear in children, it seems unreasonable to suppose that disease of the nasal sinuses should be rare in early life: for the middle ear with its Eustachian tube communicating with the pharynx is merely a specialized air sinus.

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Any or all of the accessory air sinuses may be diseased in childhood, for they are all present in early life, as will be demonstrated in the section on development. Authorities differ in their estimates of the relative frequency of disease in the individual sinuses, but the consensus of opinion seems to be that the antra are much the most often involved, then the ethmoids, and more rarely the sphenoid and frontal sinuses. The maxillary antrum offers distinct advantages to the investigator, and indeed the diagnosis apart from x-ray examination, and the treatment of infection in the other sinuses is a matter of difficulty in the young. It is for this reason that nearly all the literature upon the nasal air sinuses in children, and the direct observations in this study, are confined to the antrum.

The investigations which form the basis of this work fall into two groups. The first is a series of twenty-four children in whom the diagnosis of antrum infection was arrived at by the routine exploration of these sinuses in a hundred consecutive children. The second is composed of seventy-six children in whom the diagnosis of antrum disease was made by clinical methods, including x-ray examination.

The study of these hundred children was begun in 1932 and continued into 1933. Since that time up to the early part of 1936 these patients have been re-examined periodically, as far as it was possible to get them to attend. This series forms a useful basis upon which to build with subsequent clinical material, which has not been lacking. During the last two years the presence of antrum disease has been proved by exploratory puncture in over five hundred children attending the Aural Department of The Hospital for Sick Children.

The development of the accessory nasal sinuses.

The antrum. A pouch representing the primitive antrum can be seen on the seventieth day of foetal life. At birth the antrum is always present, but varies in size. It grows steadily, being fully developed at about fifteen years. At the age of three years it measures $22 \times 11 \times 9$ mm. (Schaeffer³). At birth the ostium is one-third to one-fifth of adult size (W. Proetz¹), but the adult size varies from 1 to 22 mm. long by 1 to 6 mm. wide (Schaeffer³). At two-and-a-half years the floor of the antrum is as much as 5 mm. above the floor of the nose; at ten years this distance is 2.5 mm. (Findlay⁵).

The frontal sinus. The recessus frontalis of the middle meatus is present at the fourth foetal month. The frontal sinus as such is always demonstrable by the end of the first year of life. At three years its cupola is higher than the nasion, and the cavity measures 5×3.5 mm. (Schaeffer³).

The sphenoidal sinus. This sinus is demonstrable as a constricted part of the nasal fossa by the fourth month of foetal life. By the third year it has become surrounded with bone and measures $5.5 \times 4 \times 2.5$ mm.

The ethmoid cells. These cells are also in evidence in the fourth foetal month, and by birth the ethmoidal labyrinth contains well-developed sinuses.

Scheme of investigation.

Proof of the presence of inflammatory exudate in an air sinus consists of aspirating such fluid from the cavity, and not of washing it out of the nose by the use of a cannula in the sinus. From the point of view of an investigation to show the frequency of antral infection in children it would be useless to examine a given number and subject to puncture only those in whom the clinical picture suggested antral disease, for the pre-conceived clinical picture might be erroneous. It therefore seemed desirable to prove the antral infection first in a number of instances, and then to work backwards to the usual clinical examination, including the use of x-rays: then having abstained from any treatment of the antrum itself to repeat the aspiration after a lapse of time in order to establish the chronicity or otherwise of the infection. This latter point assumed some importance in view of the prevalent opinion that sinus disease in childhood is transitory.

Four reasons led to a decision to aspirate the antra in a series of a hundred children undergoing removal of tonsils. First, they would have some upper respiratory complaint, possibly due to antral infection. Secondly, they could be readily punctured while under the anaesthetic, before the operation. In the third place it had been stated (Dean⁶, Mollison²) that removal of tonsils and adenoids usually resulted in the clearing up of antral infection. The fourth consideration was that in these circumstances children would not be included if they had any temporary infection such as a 'cold' which might cause exudate into the antrum.

Any antrum found to contain pathological matter (pus, muco-pus, mucus) was to be subjected to re-aspiration six months later, such a period being allowed for spontaneous recovery, or that due to removal of the tonsils and adenoids. In fact the first aspirations were made in the spring of 1932, and the second in the autumn of that year, thus allowing six good summer months to intervene.

In order to be able to compare the bacteriology of the nose with that of the healthy antrum, and with that of the diseased antrum, it was planned to take nasal swabs in a number of the cases, and to examine the contents of each of the two hundred antra bacteriologically, whether consisting of inflammatory exudate or merely returned saline.

After this preliminary series had been completed it was planned to collect a further number of children upon a clinical basis, and the study of these was to include bacteriological examination on the same lines as before, and repeated x-ray examination. Such detailed observations were stopped when a total number of a hundred cases was reached, and these children have been examined periodically over a period of from three to four years. The results of this study are set out in tables 1, 2, 3, and 4.

The technique of puncture and bacteriological examination of the antra.

The maxillary antrum of a child of any age can be punctured by a straight trocar, through the interior meatus of the nose, but as the floor of the antrum is higher than the floor of the nose, the point of the trocar must pierce the lateral wall of the inferior meatus as high up as possible, just under the root of the inferior turbinate. The trocar should be directed backwards, laterally and upwards, and on piercing the thin plate of bone immediately enters the antrum. It is not necessary to puncture through the middle meatus however young the child may be. If a simple trocar and cannula are used, and the contents of the antrum are aspirated through

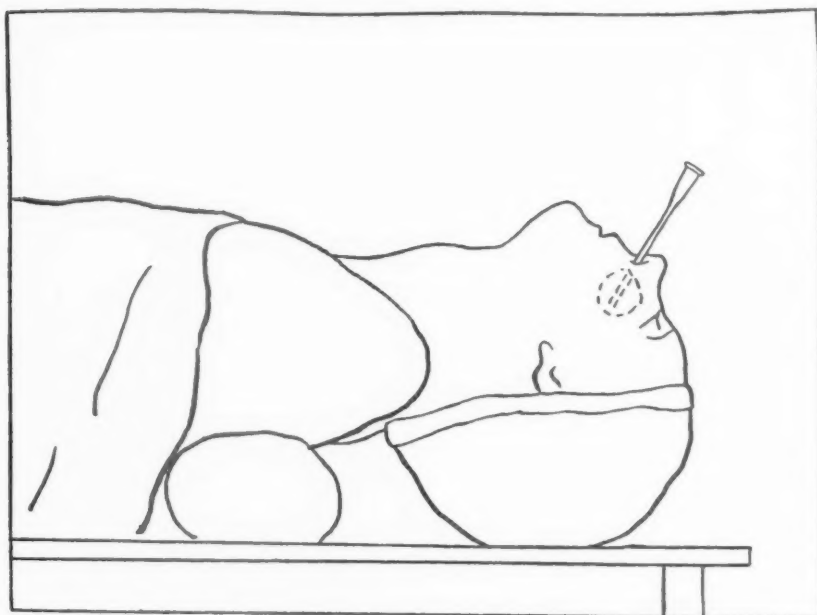


FIG. 1.—Puncture-aspiration of the antrum. This position is suitable for either local or general anaesthesia. The cannula reaches the most dependant part of the cavity, and the head is easily held still.

the cannula, they are contaminated by the inside of this tube, through which the dirty point of the trocar has been withdrawn. Therefore a finer and longer cannula attached to a glass syringe containing a few c.c. of sterile saline was passed through the original cannula left in situ, until its point touched the furthest wall of the antrum. It was then withdrawn one-eighth of an inch and the antrum aspirated. If it contained mucus, muco-pus or pus, this entered the syringe. If only air bubbles appeared it was presumably empty; 2 c.c. of saline were then injected into the antrum and re-aspirated. The saline might come back clear, or with mucus or pus. Sometimes it was impossible to aspirate air or fluid. If the cannula was in the antrum

this might be due to it being full of thick pus, or to the point of the cannula being buried in a thick mucosa.

The position of the head is obviously important, for the end of the cannula must reach the most dependent part of the antrum if the contents are not to escape aspiration. Since in a child the cannula must pass upwards as well as backwards, its point reaches the postero-superior part of the antrum, which is most dependent with the child lying on his back with shoulders on a sand pillow, and the head hyper-extended, as in the diagram (fig. 1). In this position, which was used in all aspirations, the ostium lies well up on the medial wall.

The aspirated contents of the antrum were then planted in broth and upon blood agar, and the cultures subsequently examined. In addition, the mucus, muco-pus, or pus obtained was examined directly by the microscope in a sufficient number of cases to check the naked eye observations upon the nature of the aspirated matter.

Analysis of table 1.*

ANTRUM DISEASE FOUND BY ROUTINE PUNCTURE OF A HUNDRED CHILDREN UNDER TWELVE YEARS OF AGE UNDERGOING TONSILLECTOMY.

The main fact which emerges from table 1 is that out of a hundred children having their tonsils removed, twenty-four were found to have mucus, muco-pus, or pus in one or both antra. Secondly, in only nine of these twenty-four were the antra clear of pathological content six months later, after the removal of tonsils and adenoids. Stated differently, 15 per cent. of this series of children had chronically diseased antra. The average age of the twenty-four children was seven years, thirteen were boys and eleven girls. Both antra were involved in six instances, and one only in eighteen.

Of the fifteen children (no. 1, 2, 3, 5, 7, 10, 11, 14, 16, 17, 18, 19, 20, 21, 22) who had chronically diseased antra eight (no. 2, 3, 7, 10, 11, 16, 18, 19) cleared up on antral lavage, four (no. 14, 20, 21, 22) improved, and three (no. 1, 5, 17) remained unchanged. One of these three ceased to attend, and might have improved with longer treatment. The other two have had repeated lavage, followed by antrostomy, without benefit.

That nine (no. 4, 6, 8, 9, 12, 13, 15, 23, 24) of the twenty-four children were found to have clear antra six months after tonsillectomy does not necessarily imply that their recovery was the result of this operation. It may have been; but spontaneous recovery from mild sinusitis is common.

*Tables 1 and 3 will be found at the end of this article following page 306.

TABLE 2.

BACTERIOLOGICAL FINDINGS IN 200 ROUTINE ANTRAL PUNCTURES IN 100 CHILDREN UNDERGOING REMOVAL OF TONSILS AND ADENOIDS, WITH A COMPARISON OF THE BACTERIOLOGY OF THE NASAL CAVITIES IN 45 OF THE CASES.

	Bacteriological findings in in 90 nasal swabs taken from 45 children.		Bacteriological findings in 170 antra punctured and not found to contain mucus, muco-pus or pus.		Bacteriological findings in 30 antra punctured and found to contain mucus, muco-pus or pus.	
	Number of times each type of organism was found.	Percentage for comparison (nearest unit).	Number of times each type of organism was found.	Percentage for comparison (nearest unit).	Number of times each type of organism was found.	Percentage for comparison (nearest unit).
Pneumococcus	10	7	34	17	12	30
B. pfeiffer	8	6	12	6	8	20
B. friedlander	10	7	13	6	6	15
Streptococcus	17	11	40	19	5	13
Staphylococcus	42	27	8	4	2	5
M. catarrhalis	25	16	2	1	2	5
B. proteus	0	0	0	0	2	5
B. hofmann	25	16	3	1	0	0
Sarcinae	10	7	0	0	0	0
Sterile	5 (1)	3 (1)	93	46	3	7

Each antrum is treated as a separate unit. Mixed infections were common. The figures represent the total number of times each type of organism was present.

(1) As 4 of these 5 swabs were taken on the same day the sterility may be due to a technical error.

To simplify the statements in table 2 the antra and nasal cavities are referred to as units; thus the hundred case gave two hundred antral punctures, and ninety nasal swabs were taken from forty-five of the children. The first column of figures in each section gives the total number of times the type of organism referred to was present; the second column reduces these figures to percentages to facilitate comparison between the sections. About half of the cultures showed mixed infections; in the table each type of organism present is counted.

Analysis of table 2.

THE NINETY NASAL SWABS. Many of the cultures from the nasal swabs showed mixed infections as was to be expected. Of the five swabs that were sterile four were in series upon one day, a fact strongly suggestive of a technical error. Staphylococcus was by far the most frequent organism

present, *micrococcus catarrhalis* and *bacillus hofmann* tying for second place. *Pneumococcus* was comparatively rare.

THE HUNDRED AND SEVENTY ANTRA NEGATIVE ON ASPIRATION. Ninety-three were sterile, this figure being made up of twenty-eight cases sterile on both sides, and thirty-seven sterile on one side; ten of these having mucus, muco-pus, or pus present in the other antrum. It is thus apparent that over half of the antra which were empty, and possibly healthy, were sterile. It will be shown in the discussion upon the skiagrams that many antra give radiographical evidence of disease and yet are negative on aspiration. It seems reasonable to assume that the great majority of healthy antra are sterile. The remaining seventy-seven antra which were empty, infected the saline which was injected into them and then re-aspirated. The streptococcus was the organism most frequently present, and next to that the pneumococcus. Bacilli of the Pfeiffer and Friedlander types were also numerous.

THE THIRTY ANTRA POSITIVE ON ASPIRATION. The pneumococcus was much the most frequent organism grown from the mucus, muco-pus, or pus of these diseased sinuses. Next in order was the Pfeiffer type, followed by the Friedlander bacillus. Streptococcus was also responsible for some cases, as were *micrococcus catarrhalis*, *staphylococcus* and *bacillus proteus*. The pneumococcal infections were characterized by thick yellow-green pus, usually present in large quantity.

A comparison of the bacteria found in the nose, the empty antrum, and the antrum containing mucus, muco-pus, or pus reveals a marked difference in the flora of these three. *Staphylococcus* is frequently present in the nose, rarely enters the antrum, but may cause suppuration there. The same applies to *micrococcus catarrhalis*. *Bacillus hofmann* is also common in the nose and rare in the antrum, and in no case was it associated with suppuration. Streptococcus is often found in the nose and in the antrum, and is the cause of inflammation in that sinus in a number of cases. Friedlander bacillus is more frequent in the antrum than it is in the nose, and causes suppuration. Pneumococcus is also more often found in the antrum than in the nasal cavity and is by far the most frequent cause of inflammation of the antrum in childhood. Haemolytic bacilli of the Pfeiffer type are the next most frequent cause of antrum disease although they are also comparatively rare in the nose.

An examination of the bacteriological findings in table 1 shows that upon second puncture after an interval of six months several of the antra which still contained muco-pus were sterile, whereas they had been infected at the time of the first puncture. It has been observed that organisms may die out in a long standing abscess, such as an empyema of the pleural cavity. A similar condition may presumably account for these sterile but muco-pus-containing antra. The three cases in which the muco-pus was sterile upon first puncture are open to the same explanation.

Analysis of table 3.*

SEVENTY-SIX EXAMPLES OF ANTRUM DISEASE IN CHILDREN UNDER TWELVE YEARS OF AGE.

The average age of these seventy-six children was seven-and-a-half years; thirty-eight were boys and thirty-eight girls; both antra were involved in fifty-five, and one only in twenty-one. The tonsils and adenoids had been completely removed previously in forty-one.

From a clinical point of view they can best be divided into three classes: those who were cured after treatment, those who improved, and those who failed to benefit.

CURED. (No. 26, 29, 31, 32, 33, 34, 36, 38, 39, 40, 42, 43, 44, 48, 49, 50, 52, 54, 55, 56, 58, 65, 68, 70, 71, 72, 75, 77, 78, 79, 80, 82, 84, 86, 89, 96, 100.)

Thirty-seven of the seventy-six children could be classified as cured after treatment. In twenty-six of them a final skiagram showed the antra to be clear, not only of fluid content, but of residual mucosal thickening; in three it was doubtful if the x-ray was quite clear; in two it was still positive, showing thickening of the mucous membrane although the children were perfectly well. Final x-rays were not taken in six instances as the children failed to attend.

The antra were clear on final lavage in twenty-four of the thirty-seven: seven were free from symptoms and had negative skiagrams, and repeated puncture did not seem justifiable; six failed to attend, but were reported to be well.

The tonsils and adenoids had been removed previously in eighteen of these thirty-seven children: in five they were removed during the treatment, including two with remnants; in fourteen they were still present at the end of treatment, eight being healthy, three infected, and three remnants.

The surgical treatment of thirty-five of the thirty-seven was antrum lavage, the average number of washes being between two and three. Intra-nasal antrostomy was performed on two.

IMPROVED. (No. 25, 27, 28, 35, 46, 47, 51, 57, 59, 61, 62, 63, 67, 69, 73, 74, 76, 81, 83, 85, 87, 90, 91, 92, 97, 99.)

Twenty-six of the seventy-six children were improved by treatment. They include one with a doubtfully clear skiagram, who still had nasal discharge, thirteen whose x-rays still showed pathological changes in the antra and twelve who had not attended recently for x-ray examination, but were improving clinically when last seen.

Of the twenty-six, seven were clear on final lavage, and six had intra-nasal antrostomy performed. The others were treated by lavage, and improved, but the washes were never clear.

The tonsils and adenoids had been removed previously in seventeen: in three they were removed in the course of treatment, including one with remnants; in five they were still present when last examined, three being healthy, one infected, and two remnants.

*Tables 1 and 3 will be found at the end of this article following page 306.

NOT IMPROVED. (No. 30, 37, 41, 45, 53, 60, 64, 66, 88, 93, 94, 95, 98.)

Thirteen of the seventy-six children were not improved by treatment. X-ray examination still showed gross pathological changes in nine of the thirteen: the other four failed to attend.

Repeated lavage failed to give any benefit to six: lavage and antrostomy failed in four: one was clear after two washes, but the symptoms have recurred: one improved locally on lavage, but the symptoms were not relieved: one was not improved by one wash and ceased to attend.

The tonsils and adenoids had been removed previously in five of these children, and in four they were removed in the course of treatment. They are still present in four instances, and are unhealthy in three of these.

TABLE 4.

BACTERIOLOGICAL FINDINGS IN 161 ANTRA OF 100 CHILDREN ASPIRATED AND FOUND TO CONTAIN MUCUS, MUCO-PUS OR PUS.

	Bacteriological findings in 30 antra of 24 children of table 1.	Bacteriological findings in 131 antra of 76 children of table 3.	Bacteriological findings in antra of children in table 3 arranged according to clinical results.		
			Cured.	Improved.	Not improved.
Pneumococcus	12	58	28	20	10
B. Pfeiffer	8	32	14	12	6
B. Friedlander	6	3	2	1	0
Streptococcus	5	19	8	4	7
Staphylococcus	2	4	1	3	0
M. catarrhalis	2	0	0	0	0
B. proteus	2	0	0	0	0
B. Hofmann	0	3	1	1	1
Sarcinae	0	0	0	0	0
Sterile	3	39	19	15	5

Each antrum is treated as a separate unit. Mixed infections were common. The figures represent the total number of times each type of organism was present.

Analysis of table 4.

Again in this table the figures represent the total number of times each type of organism was found. The infection was often mixed, and there would seem no way of determining the degree of responsibility for inflammation attaching to one or other of, say, three types of organism found in one antrum. It is assumed that the organism most often found in association with antrum infection is the one most likely to cause such an infection.

The bacteriological findings in group 1 of twenty-four children closely resemble those of group 2 of seventy-six children. The pneumococcus was much the most common organism found in the series, but Pfeiffer's bacillus was also frequent. It is interesting to note the presence of the latter bacillus in quite a number of consecutive cases occurring in March, 1933,

as shown in the second half of table 3. In group 1 the Friedlander organism was common, but not in group 2. The streptococcus was common in both groups. The number of sterile cultures was high in group 2, and it is thought that this may have been due to a technical difficulty in planting out the aspirated matter for culture as soon after aspiration as in group 1.

The right hand half of table 4 sets out the bacteriological findings of the seventy-six children of group 2 in sections according to whether the patients were cured, improved, or not improved. As far as can be deduced from the limited figures, streptococcal infection of the antrum would seem to be more resistant to treatment than that due to the pneumococcus or the Pfeiffer bacillus.

Pathology and bacteriology of sinusitis in childhood.

In considering the causation of sinusitis, the primary fact to be kept in mind is that the mucous membrane lining the sinuses is in one piece with that lining the nasal cavity. It is impossible to have inflammation in the latter without some spread to the former. A skiagram of the sinuses taken during any nasal 'cold' will show some thickening of their mucosa. Although the sinuses are more shut off from the stream of air-borne organisms than is the nose, they are at a disadvantage to the nasal cavities in that, once infected, it is more difficult for them to rid themselves of the products of the inflammation. Their ostia are small, and in the antra badly placed for drainage. Since the cilia of the sinuses work towards the ostia dependent drainage is not normally necessary. When they are weakened by inflammation, and have a large mass of muco-pus to move, they may fail to expel it through a small opening, itself reduced in size or closed by surrounding congestion. Retained exudate acts as an irritant, and further mucus or pus is poured forth, a vicious circle of retention being set up.

The health of the lining membrane of the sinuses is also dependent upon proper ventilation. This requires free passage of air through the nose, and the changes of air pressure in the sinuses which result. Should the nasal airway be blocked, for instance by a large pad of adenoids or a deviated septum, the sinuses may cease to drain owing to feeble ciliary action.

These mechanical factors play a large part in the causation of sinusitis, and particularly so in children. The ostia of the cavities in the young are smaller than in the adult, but the mucus or pus produced is of the same consistency. The child's nose is also smaller, and more easily blocked, and enlargement of the adenoids is more frequent.

The common clinical conditions giving rise to sinusitis are 'colds,' influenza, and the infectious fevers, particularly whooping cough. Bathing in infected water is another frequent cause. It has been notable that in a number of children with sinusitis the symptoms have arisen following removal of the tonsils and adenoids. In the writer's view this is not due to loss of the lymphoid tissue of the throat, but to the sinuses becoming filled with infected blood at the time of operation, from lack of adequate

technique in the control of haemorrhage. The blood clots in the sinus and sets up inflammation there. The child's antrum is free from one of the dangers of infection which beset that of the adult. Infection from the teeth must be rare, for the roots do not project into the floor of the antrum, separated only by a thin plate of bone, as they do in later life.

The bacteriology of antrum infection has been discussed with tables 2 and 4. The pneumococcus was shown to be the organism most frequently present: the muco-pus or pus which it produced was characteristically thick and green-yellow in colour, so that it became possible to suspect its presence by the nature of the matter. Perhaps the thickness of pneumococcal pus is a factor in the prevalence of this coccus in sinus infection: the cilia find it more difficult to extrude than a less viscous fluid. No doubt the bacteriology of sinus inflammation varies with the type of naso-pharyngeal infection prevalent at the time it arises. E. Watson-Williams⁷ has recorded observations to this effect. In the present series the Pfeiffer bacillus was next most frequent. The streptococcus took third place, and would seem to affect the prognosis adversely.

Something is known about the mechanical and bacteriological factors in the causation of sinusitis. Of the more important factor, the lack of resistance of the individual to infection, hardly anything is known. Some children seem to be unable to resist any infection of the respiratory tract. The typical example is the child who catches cold almost continuously, has repeated attacks of bronchitis, and by the age of ten years or so has well marked bronchiectasis. An x-ray of the sinuses of such a child will show pathological changes in the antra in almost every case. It has been shown that deficiency in diet of vitamin A results in sinusitis in rats⁸. A like deficiency in the human being is also known to undermine the resistance to infection. That this is not the only factor is obvious.

Sinusitis is likely to be common in those climates where upper respiratory infections are frequent. A cold damp sunless atmosphere is particularly likely to induce nasal infections, and sudden changes of temperature, such as result from entering a centrally-heated room from cold outside air, cause nasal congestion.

Finally the allergic state may lead to sinusitis. The rhinitis which is typical of this condition results in great swelling of the mucous membrane lining the nose and sinuses, and the outpouring of a large quantity of mucus. The ostium of an air sinus is easily occluded temporarily, and the exudate retained: it may become infected secondarily. The muco-pus aspirated from an allergic sinusitis contains a high proportion of eosinophils.

The pathological changes which occur in the lining of the sinuses in childhood range from mild catarrhal oedema to suppuration and destruction

of the epithelium, as in sinusitis generally. Polypus formation, however, is not common. The bone surrounding the sinuses in the very young is more porous than in later years, and this is reflected clinically in a greater tendency to osteitis due to infection spreading from the air cells.

It must be emphasized that the lining membranes of the sinuses is in reality one of the coverings of the body, and that bacterial infection and the production of pus in a sinus is not comparable, for instance, to infection in a long bone; it is strictly speaking outside the body. In general, it may be stated that the acute manifestations associated with suppuration inside the body do not occur in sinusitis unless there is a lesion in the continuity of the mucous membrane, or blocking of an ostium with accumulation of pus under pressure. On the other hand, chronic sinusitis, even with adequate drainage of discharge, is a common cause of general, and perhaps particularly mental, debility.

The nature of the lymphatic drainage from the sinuses would appear to have a direct bearing upon these observations. Mullin and Ryder⁹ state that there is little absorption from the uninjured mucosa of the sinuses. There is a free anastomosis of the lymphatics of the sinuses and of the nasal mucosa: they drain to the internal jugular and retro-pharyngeal glands, and also to the sub-maxillary group.

The incidence of sinusitis in children.

Observations upon the incidence of sinusitis, or more accurately of antrum infection, by routine antrum puncture of children who are undergoing tonsillectomy have been recorded by various authors; their figures correspond fairly closely with those in table 1. Compared to the 24 per cent. found there Mollison and Kendall² found 22 per cent. of children with muco-pus or pus in their antra. J. W. Carmack¹⁰ examined all patients admitted to a hospital and found muco-pus in the antra in 12 per cent. of ninety-six in 1927: 14.2 per cent. of 328 in 1928. In 1930 he examined only those children who were to have their tonsils and adenoids removed, and he found 30 per cent. positive. Harke¹¹ examined the sinuses of 394 children post mortem, and found sinusitis in sixty-two, fifty-two of them being between nine months and fifteen years of age. The maxillary antrum was involved in forty-seven, the ethmoid labyrinth in three, and the sphenoid in two. His findings are of value in confirming the clinical observation that the antrum is much more frequently diseased than the other sinuses. In the Aural Department of The Hospital for Sick Children, muco-pus or pus has been washed out of the antra in over 500 children during the last two years. There can be no doubt that sinusitis in childhood is common,

The clinical manifestations of sinusitis in children.

Nasal discharge (84 of 100 children). In group 1, twelve of twenty-four children give a history of nasal discharge; and in group 2, seventy-two of seventy-six were found to have either anterior or posterior nasal discharge. The difference in proportion is explained by the different means employed to collect the cases, and by a growing realization that many mothers of the hospital class regard nasal discharge as normal; they even regard otorrhoea a commonplace. In addition anterior nasal discharge is a source of trouble to a child: his mother may attack him with a handkerchief. He therefore frequently prefers to convert it into post-nasal discharge by sniffing, and his mother fails to realize the origin of the throat cough which develops. The discharge is more or less continuous; it may clear up in dry weather, and when the child is above his normal general state. It recurs with each cold, and is then particularly profuse. It persists in quantity for weeks after a cold. The average duration of the discharge in the eighty-four children was two years. If the sinusitis is unilateral it is often possible to get a history of one-sided nasal discharge, but not always. The discharge may be mucoid, mucopurulent, or frankly purulent. It is often accompanied by crusting in the nose and excoriation of the nostrils with consequent nose-bleeding. The infection may spread up the naso-lachrymal ducts and cause conjunctivitis with purulent discharge.

Colds (83 of 100 children). Even in this country an unusual susceptibility to colds is indicated by 83 per cent. of these children suffering from them frequently. The mothers often stated that they were never free from colds. That may be another way of describing continuous nasal discharge. Each fresh cold is accompanied by an exacerbation of the signs and symptoms, such as profuse nasal discharge, barking cough, headache, and nasal obstruction. As each cold causes more inflammation in the sinuses, and chronic sinus infection leads to colds, the vicious circle is complete. It is reasonable to assume that the organisms harbouring in a chronically infected sinus are ever ready to avail themselves of a lowering of the local or general resistance to extend their activities to the nose and throat. A cold, or tonsillitis, is an occasional result of sinus lavage, the bacteria being released from their lair.

Cough (82 of 100 children : 44 had had bronchitis). The cough which is the result of sinus disease without any lesion in the chest must be considered by itself in the first place. It may be simply a throat-clearing cough, or so violent as to simulate the paroxysms of whooping-cough. Sinusitis is one of the causes of 'croup.' Such coughs are the result of pharyngeal irritation and inflammation from infected post-nasal discharge. Secondly,

attention must be drawn to the close relationship between pulmonary inflammation and sinus disease. In most cases of pulmonary fibrosis or bronchiectasis the para-nasal sinuses will be found to be diseased¹². There are three possible explanations of this. The sinus infection may be primary, and the discharge which results, passing down the respiratory passages to the lungs, chiefly during sleep, may set up inflammation there. There is no lymphatic communication between the sinuses and the lungs⁹. The coughing-up of infected matter from the lungs may infect the sinuses. Lastly, and this seems the most probable, there may be a general inability of the respiratory system to resist infection, whether in the sinuses or in the lungs.

Cough which results from the sinuses alone responds rapidly to treatment of the local condition. Attacks of bronchitis have been observed to be less frequent after such treatment when the patient suffered from both sinusitis and bronchitis. J. P. Findlay⁵ reports thirty-six cases of pulmonary inflammation in childhood improved by the operation of antrostomy.

Sore throat (25 out of 100 children). In the first group of twenty-four children, all with tonsils and adenoids present but presumably requiring removal, ten gave a history of sore throats. In the second group of seventy-six children, only thirty-five had not had their tonsils and adenoids completely removed before they were found to have sinusitis. Of these thirty-five, twelve suffered from sore throat. Since many of these sore throats may have been a direct result of tonsillar infection, it would not seem that sinusitis is a common cause of sore throat. It is a cause of an irritable 'dry' throat, but such a complaint is not made by children. Tonsillitis sometimes results from antrum lavage.

Cervical adenitis (37 of 100 children). Of the hundred children fifty-nine had their tonsils and adenoids present when they were found to have sinusitis. Of these, twenty-eight had enlarged anterior cervical glands. The tonsils and adenoids had been completely removed in forty-one, and only nine of these were found to have enlarged glands. The glands into which the sinuses drain are the deep jugular, or retro-pharyngeal glands, and the sub-maxillary glands. Palpation of the sub-maxillary glands, and inspection of the pharyngeal wall has not impressed the writer with the frequency of glandular enlargement in sinusitis. Even in acute inflammatory conditions of the sinuses he has been struck by the absence of corresponding adenitis. This clinical observation is in accord with the conclusion of Mullin and Ryder⁹ that there is very little absorption by the lymphatics of the sinuses. Reisman¹³ makes contrary clinical observations.

Snoring and mouth breathing (62 out of 100 children). To clarify any conclusions from these figures, those children who still had their tonsils and adenoids present should be excluded. Of forty-one children with sinusitis who had had their tonsils and adenoids completely removed previously, twenty-two still suffered from nasal obstruction. This was the result of congestion and swelling of the nasal mucosa together with the presence of discharge in the nose. The nose is a narrower air-channel than the nasopharynx. It is not common to find adenoids so large that they reduce the size of the naso-pharyngeal air-way to less than that of the inspiratory glottis, a necessary condition if they are to cause respiratory obstruction. It is common to find a nasal air-way reduced to the merest chink as a result of swelling of the mucosa and secretion. The 'adenoid facies' is more often the result of naso-sinusitis than of adenoids.

Headache (44 out of 100 children). Headache is not a common complaint in childhood, and its occurrence should arouse suspicion of sinusitis. It was frequent in the series detailed, and this experience has been supplemented more recently. On a number of occasions a search for the cause of headaches in a child has led to the discovery of sinusitis, with subsequent cure by treatment. The headache is usually frontal, even if the antrum is at fault; is often to one side, and is present on several consecutive days, perhaps following a cold. It may present the characteristic daily periodicity.

Otitis media (44 out of 100 children). Recurrent or chronic otitis media is frequently the result of sinusitis. The infected post-nasal discharge runs down over the orifices of the Eustachian tubes and causes inflammation there, which may spread to the ear. As a cause of otitis media sinusitis is only second to adenoid infection, and should always be suspected if removal of adenoids has not resulted in freedom from such attacks. Catarrhal deafness may be dependent on sinusitis, and a return to normal hearing has been effected by antrum lavage in a number of children.

Systemic manifestations. Although sinusitis may exist with apparently excellent general health, the majority of children suffering from it are in poor condition. This may be the cause or the result of the sinusitis, but there is a clinical picture suggestive of the condition. The child is tired and pale, with dark rings under the eyes: he finds it difficult to concentrate, and loses interest in work and play. Also characteristic is a change for the worse in temperament, and instead of being a happy, sunny child he becomes morose, ill-tempered, and difficult to manage. There was great hope that the sinuses would prove to be a common site of focal infection in those diseases such as arthritis and nephritis, which may depend on such a focus. In few cases has this hope been fulfilled, although of recent years at The Hospital for Sick Children, examination of the sinuses has been extensively carried

out in such conditions. Two examples of haemorrhagic nephritis depending upon antrum infection have been observed. They both responded rapidly to lavage. It should be recalled that pus in a sinus is strictly speaking outside the body, and that the lymphatic absorption from the mucous membrane is slight.

The individual sinuses.

THE MAXILLARY ANTRUM. This sinus is much more frequently the seat of disease than the other sinuses in childhood. The inflammation is usually of a subacute or chronic type. Rarely does acute suppuration with closure of the ostium, pain, tenderness, swelling of the cheek and eye, and acute toxæmia develop. Commonly there is mucoid exudate as a result of catarrhal inflammation: in more severe examples the discharge is mucopurulent. Sometimes pus is produced, and destruction of the lining epithelium, with fibrosis of the sub-mucosa results. Polypus formation is rare in the young. Osteitis of the maxilla may be due to the spread of acute infection from the mucosa, particularly in the first two or three years of life.

THE ETHMOIDAL SINUSES. Ethmoiditis is probably second to antrum infection in frequency. The inflammation is usually catarrhal, and such a condition is a not uncommon cause of long-continued mild nasal congestion and discharge. Acute suppuration in the ethmoidal cells in very young children is occasionally encountered. The baby is very ill, with high fever and toxæmia. The corresponding orbit is greatly swollen, and the movements of the eyeball are limited or abolished by external pressure; the eyeball may be proptosed. The swelling extends into the upper part of the side of the nose, and this area is tender on pressure. Such a condition has been mistaken for cavernous sinus thrombosis, and indeed this serious complication may arise with a fatal result.

FRONTAL SINUS. Inflammation of this sinus is not very common in childhood. The development of the frontal air-cell varies greatly, both in the individual, and comparing one side with the other. Headache is a prominent symptom in disease of this sinus. It may be of the vacuum type, due to blocking of the long and narrow sinus duct, or a result of increased pressure from retention of exudate. Suppurative inflammation in the young, requiring surgical interference, is outside the writer's experience.

SPHENOIDAL SINUS. Apart from general naso-sinusitis inflammation in this sinus is rare in childhood. Sphenoid suppuration, which led to cavernous sinus thrombosis, was the cause of death in a child at The Hospital for Sick Children.

Diagnosis.

The diagnosis of sinusitis depends upon recognition of the clinical manifestations, together with certain special examinations. These are inspection of the nose and throat, x-ray examination, transillumination, and puncture-aspiration.

Examination of the nose and throat. This must of necessity be made with a forehead light and with the use of nasal specula of a suitable size for children. Although surprisingly enough sinusitis may exist with little that is abnormal to be seen in the nose, typically the presence of infected discharge results in congestion and swelling of the mucous membrane of the corresponding side. The antrum, the anterior ethmoids, and the frontal sinus all open into the middle meatus of the nose, and exudate from them runs over the inferior turbinate. Muco-pus or pus may be seen in the middle meatus, or accumulated in the inferior meatus. The inferior turbinate is large and red and moist. Sometimes the discharge forms crusts in the nose, and the mucous membrane may be fiery red but dry. In ethmoiditis the middle turbinate may be swollen, so that it presses on the septum. A swollen pale nasal mucosa will suggest allergic rhinitis, not only as a cause of the nasal condition, but possibly the primary source of the sinusitis. Crowding of the nose due to septal deviation or spurs has been mentioned as a possible cause of sinusitis. Such conditions should be noted, but they have played a very small part in the cases recorded here. If the child will submit, posterior rhinoscopy should be carried out. Examination of the throat may reveal post-nasal discharge, either running down the pharyngeal wall, or hanging in a blob behind the uvula. Hypertrophy of the granular lymphoid follicles of the posterior or lateral pharyngeal wall results from infected post-nasal discharge, and should suggest sinusitis.

X-ray examination of the sinuses. This is the most sensitive of all the diagnostic tests for sinusitis (fig. 2, 3, 4). Not only will it reveal gross pathological changes, but it may show a slight and transitory swelling of the mucous membrane. It is of great value, but equally it can prove misleading if not correctly interpreted and co-related with the clinical condition. It has already been mentioned that a common cold running its uncomplicated course produces 'opaque antra,' and allergic swelling of the mucous membrane will show in an x-ray film. Should there be only slight change in the lining membrane as a result of inflammation, but a free production of muco-pus or pus, a fluid level will be shown. If the mucosa is thickened or fibrosed from inflammation, but there is no retention of exudate, an air-space will be seen in the centre of the shadow cast by the membrane, unless it is so dense as to render the whole area of the sinus opaque. Usually there is a thickening of the lining membrane and retention of some muco-pus, and then the shadows so merge together that the sinus in question shows a more or less uniform opacity in the skiagram. It may be safely stated that if a good skiagram of a sinus is clear there is no disease



FIG. 2A.—Date 11.1.32.

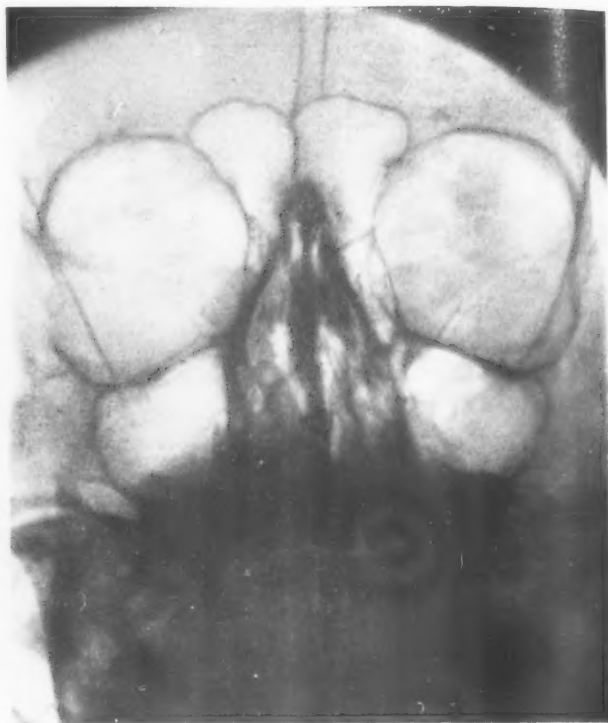


FIG. 2B.—Date 3.10.32.



FIG. 2C.—Date 9.11.35.

No. 54.—Table 3.

Nasal discharge, cough, colds, headaches for one year. Muco-pus washed out of right antrum 16.1.32. Since then has been free from symptoms.

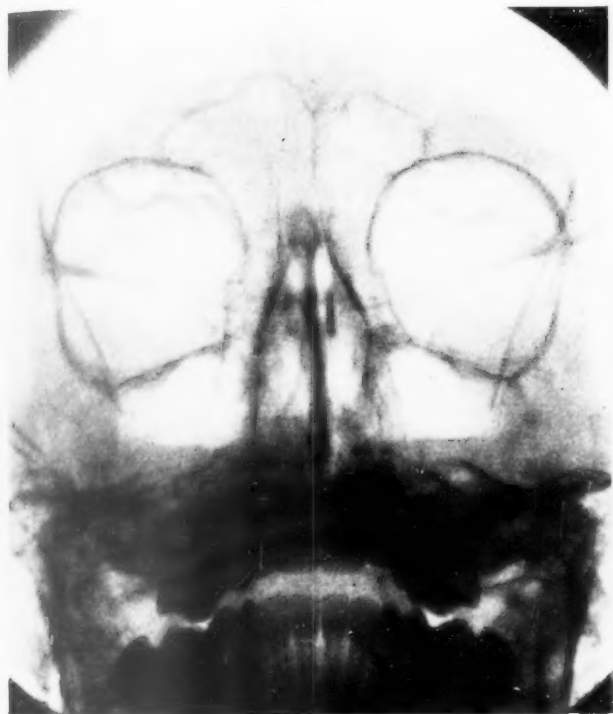


FIG. 3A.—Vertical position.



FIG. 3B.—Tilted position.

Muco-pus in the antra of a girl aged $9\frac{1}{2}$, showing fluid level, demonstrated by tilting. This child suffered from 'allergic naso-sinusitis.'



FIG. 4.—Opacity of the right frontal sinus, right ethmoids, and right antrum in a boy of 9.

present. The writer has never obtained muco-pus from an antrum clear to x-rays, and it may be recalled that many antra which proved so to be were aspirated in the course of collecting the children in table 1. Wasson's assumption¹⁴ that the contrary would prove to be the case can be discounted. On the other hand, it is common to wash out an antrum which is opaque to x-rays, and obtain a clear result. The sinus is diseased none the less, but is draining adequately. Bearing in mind the value of a clear skiagram, it was satisfactory to find so many of the children studied in this series negative to x-rays after treatment. Much information may be obtained from one x-ray film taken in the upright position with the head thrown back, so that the nose and the chin lie in the vertical plane. A good view is obtained of the antra and frontal sinuses, and the ethmoids are displayed to some extent. The complete x-ray examination of the nasal sinuses requires exposures in several positions. Dr. Bertram Shires kindly undertook all the radiological work to which reference has been made here.

Transillumination. Transillumination is not so accurate as x-ray examination, and in childhood special difficulties make it even less reliable. Poor transmission of light may be due to pathological changes in the sinus in question, but may also be the result of relatively late development; in the case of the antrum in which transillumination is normally of most value, unerrupted teeth may cause opacity. X-rays will differentiate between these conditions: transillumination cannot.

Puncture aspiration. The technique of antrum puncture and aspiration has already been described. Although a positive x-ray will serve to make a certain diagnosis of disease in a sinus, the presence or absence of fluid content can only be proved by puncture-aspiration. In addition an opportunity is afforded of discovering the organisms causing the infection. The antrum is the only sinus which is readily accessible to this investigation. Therapeutic lavage will usually be carried out immediately after aspiration, through a cannula left in situ.

Treatment.

Acute sinusitis. It must be emphasized that some degree of sinusitis occurs with every cold. The vast majority of such inflammations settle spontaneously. When a cold hangs about for several weeks the fault usually lies in failure of drainage of one or more of the sinuses. Even then there will usually be no need to resort to surgical treatment, although in the case of the antrum, lavage may be the most expeditious means to recovery. The proper treatment of the cold itself will go a long way to prevent such sequelae as sinusitis and otitis media. The child should be kept in bed, or in a warm well-ventilated room. Sudden changes in temperature are prone to cause nasal congestion. Blocking of the nasal airway should be prevented

by the use of mild shrinking drops. The nasal antiseptic oils, of which so many proprietary preparations exist, are usually too strong for a child, and cause pain on introduction. They should be diluted with liquid paraffin, and a prescription should not contain more than 1 per cent. of mixed volatile oils, and $\frac{1}{2}$ per cent. of ephedrine. The latter is very irritating to some noses. In addition if possible the child should be made to inhale the vapour of menthol or compound tincture of benzoin. Proper nose blowing is important. The nostrils must not be compressed while blowing out. The increase in intra-nasal pressure which results forces matter into the sinuses. The handkerchief should be held loosely round the nose while the child blows down, and the nose subsequently wiped. If the cold still lingers on after a week or two, a holiday, preferably at the sea-side, should be arranged. If that fails, then the point has been reached where surgical treatment of the sinuses may be necessary.

When an upper respiratory infection is more virulent, acute catarrhal or suppurative sinusitis may arise even in the early days of the illness. Should an ostium become blocked there is retention of the products of inflammation with toxic manifestations, severe headache, localized tenderness and perhaps swelling. Treatment in the first place is conservative, an attempt being made to get the sinus to discharge by the use of nasal drops, inhalations, and the local application under vision of 10 per cent. cocaine and adrenaline to the middle meatus of the nose, to reduce congestion. Fortunately aspirin alone often controls the headache. The warmth of short-wave diathermy applied to the nose is comforting, and often beneficial. Such measures are usually rewarded by a discharge of pus from the sinus, and rapid improvement in the symptoms. If they fail, the next step depends on the particular sinus involved. The antrum should be aspirated, but not washed through until the acute process has settled. Acute suppuration in the ethmoids has been described. It calls for an external operation to drain the cells.

Chronic sinusitis. All the children in tables 1 and 3 fall into this category. Should the discharge be mucoid the condition is labelled catarrhal. When pus is produced suppurative sinusitis is present. The two conditions merge into each other. In treating chronic sinusitis the importance of correcting environmental and dietetic errors cannot be overestimated. Local treatment is on the whole successful, but it should be supplemented by general measures. Lavage may clear up an infected antrum, but if the factors responsible for its origin are not removed there can be small wonder if it recurs. A good diet and a few months at the seaside can establish a cure which could not be made permanent by local treatment only; in some instances they alone will suffice, without surgical interference.

The use of nasal antiseptic oils and inhalations is helpful. The nose is thereby rendered less congested, and the sinuses are given a better oppor-

tunity to drain. It is doubtful if such oils ever reach the sinuses themselves, unless special means such as 'displacement' are adopted.

In the majority of cases the sinus inflammation results in, and depends to some extent upon, the retention of the products of infection in its cavity. That the repeated removal of such exudate frequently leads to resolution of the pathological process has been demonstrated clinically beyond doubt, and is reaffirmed by a study of the results of such treatment of the children in this series. The sinus involved in these examples was the antrum, which lends itself to lavage, and forty-three of the hundred children were cured by this means, and a further twenty-three improved. The average number of washes was between two and three, usually at weekly intervals. They were repeated until the result was clear. Subsequently a number of children have had six, eight or even ten weekly washes, with gradual improvement.

In the Aural Department of The Hospital for Sick Children antrum lavage is carried out under local anaesthesia, even in the youngest patients. Only in exceptional circumstances is it found necessary or advisable to employ a general anaesthetic. Cocaine is used, and no disturbing toxic manifestations have resulted from it on well over a thousand occasions. A wisp of cotton-wool is wound round a thin wooden nasal stick, and dipped in 10 per cent. cocaine and 1 in 1,000 adrenaline, equal parts. Excess of solution is squeezed off. The stick is then inserted below the inferior turbinate under vision. If correctly placed it is firmly gripped, and remains pointing laterally as well as backward. It is left in position for half an hour. The child is then laid on his back with the shoulders on a sand pillow, and the head extended. A nurse holds the head with a hand on each side, and the surgeon sits at the end of the table. Such a position prevents the greatest difficulty in antrum puncture in the young—movement of the head away from the surgeon. The point of the trocar must be well up under the root of the inferior turbinate, and is directed backwards, upwards and laterally. When the cannula is in position the antrum is aspirated, and then the child is sat up for lavage. He leans over a basin, and warm sterile saline is syringed through the cannula. It runs out of the nose into the basin taking with it the contents of the antrum. Finally, the sinus is filled with air, and then the cannula withdrawn. No evil effects have followed this procedure if an occasional cold or sore throat, attributed to the release of virulent organisms from the antrum, are excepted.

Direct lavage of the ethmoids and frontal sinuses in a similar manner to the antrum is not possible. A few years ago Proetz¹⁵ introduced his 'displacement method' of treating sinusitis. It is applicable to all the sinuses, but in the case of the antrum, lavage is easier and more efficient.

Briefly, displacement consists in filling the nose with a therapeutic fluid and then subjecting it to repeated negative pressure. Air bubbles out of the sinuses, and the liquid runs in to take its place. A solution of $\frac{1}{2}$ per cent. ephedrine in normal saline is commonly used. It causes shrinking of the mucosa of the sinuses, and renders their ostia more patent. The method is readily applicable to children, and the results in ethmoiditis are certainly good.

In chronic suppurative sinusitis it may be necessary to make a large artificial ostium at a dependent point so that a sinus may drain into the

nose. This should only be done if repeated lavage or displacement fails. In the hundred cases of antrum disease described previously this procedure intranasal antrostomy was resorted to in eleven instances: of these two made complete recoveries, six were improved, and three remained unchanged.

The operation is performed under general anaesthetic, after shrinking the nose. The inferior turbinate is fractured upwards, and as large an opening as possible is punched out between the inferior meatus and the antrum. Good ventilation of the air cell is attained, and if necessary lavage is easily carried out by a curved blunt cannula.

In advanced suppuration of the antrum with degeneration of the mucous membrane, a Caldwell-Luc operation may be necessary.

Chronic ethmoiditis may demand the opening of the ethmoid labyrinth, but in childhood this should only be done if there is necrosis of bone.

Some success has attended the use of autogenous vaccines prepared from organisms grown from sinus aspiration.

Prognosis.

Of a hundred children, fifty-two were cured, thirty-two improved, and sixteen remained unchanged. The results in these hundred children give a fair picture of the degree of success which has attended the treatment of greater numbers subsequently. In estimating the prognosis, two important factors must be considered; first, the degree of pathological change in the sinuses, and secondly, the general condition and environment of the child. The infecting organism may have a bearing on the question, and it has already been suggested that streptococcal lesions are more resistant to treatment. Anatomical deficiencies, and other pathological states in the nose and throat affect the prognosis. A nose which is unable to function normally owing to the presence of an enlarged or infected pad of adenoids, or of a deviated septum, or because it is itself small and crowded, will make the prognosis less good, if the defect is not rectified. Similarly a sinus which has an unusually small ostium is at a disadvantage.

A complete cure can be anticipated in about half of the children suffering from chronic antrum infection. Many of them will have had symptoms of sinusitis for many months, or even a few years, following upon repeated colds or one severe cold, influenza, whooping cough, or some other infection. On washing out the sinus in question muco-pus or pus is obtained. There is a gradual improvement following each lavage, the result becoming less purulent and more mucoid, until eventually it is clear. In obstinate cases washing may be necessary every week for a month or two. An x-ray taken at the end of treatment will still be opaque. It takes some time for the mucosa to return to normal even after it has ceased to be actively inflamed. Sometimes the result of a single wash is a dramatic cessation of symptoms which may have been present for many months. Probably the explanation

of such satisfactory cases is that the antrum has harboured a clot of mucus too big to escape normally from its ostium. The presence of the clot keeps up irritation of the mucosa, and discharge. Its removal is followed by immediate recovery of the mucous membrane which was not grossly infected but merely irritated mechanically. Of the fifty-two children who recovered completely, seven belonged to the first group and their antra were clear six months after tonsillectomy, without other local treatment. They represent either spontaneous recovery, or recovery as a result of removal of the tonsils and adenoids. They are not comparable to the second group where the diagnosis was made by clinical observation.

In about one-third of children suffering from antrum infection, improvement but not complete cure is attained. They will generally be found to suffer from one of the disadvantages mentioned previously; poor general condition, bad environment, a virulent or long-standing infection, or some other debilitating factor in the nose or throat. In this category were thirty-two of the hundred children. They were usually well for a week or two after a course of lavage, but their symptoms recurred whenever they caught a cold. Some of them remained quite free from some of their symptoms, while retaining others.

A certain number of children with sinusitis resist every method of treatment which has been adopted. There were sixteen such children in the hundred. This number might have been less had they attended regularly for treatment, but as far as it went it was doing them no good. The degeneration of the mucosa of their antra may have been so advanced that nothing short of its complete removal by the Caldwell-Luc method would suffice. The writer hesitated to resort to this operation in such young subjects, and probably erred on the side of caution. If the opportunity were there they would all be sent to some far-off, dry, sunny climate for a year. They could be no worse, and might be much better.

The relationship between sinusitis and infection of the tonsils and adenoids.

For many years attention has been focussed upon the tonsils and adenoids as the centre of pathology in the nose and throat of children. Probably this is as it should be, and there is no operation of choice in surgery rewarded with such satisfactory results as removal of tonsils and adenoids properly performed for correct indications. On the other hand, there can be no doubt that much illness arising in the nose and throat for which the tonsils and adenoids were not responsible, has been laid at their door. An attempt has been made in this paper to demonstrate the frequency of sinusitis in childhood, and to draw attention to the clinical picture which should arouse suspicion of its presence.

Two questions come to mind. Are infected tonsils and adenoids the usual cause of sinusitis in childhood? If so, it must be as a result of

adenoids so large as to interfere with nasal ventilation, or of surface-spread of infection from the pharynx to the nose, against the normal mucus stream kept up by the cilia. The removal of tonsils and adenoids should result in the cure of sinusitis; and sinusitis should not be common among children whose tonsils and adenoids have previously been removed. It has been shown in table 1 that of twenty-four children with mucus, muco-pus or pus in their antra, only nine cleared up following removal of the tonsils and adenoids, and it is reasonable to suppose, bearing in mind the means of diagnosis of these cases, that some at least would have done so without operation. Table 3 demonstrates that of seventy-six children with sinusitis, forty-one had previously had their tonsils and adenoids completely removed. The broad conclusion is justifiable that infection of the tonsils and adenoids is not the common cause of sinusitis in childhood, and that their removal is neither a preventive or cure of the condition.

Is inflammation of the para-nasal sinuses a common cause of infection of the tonsils and adenoids? As the flow of post-nasal discharge is directed over the adenoids and posterior halves of the tonsils, the mechanical possibility of their infection from the sinuses is evident. If such an infection takes place, children with sinusitis should have diseased tonsils and adenoids. It is very difficult to draw conclusions upon this point from the cases studied here. Of the seventy-six children in table 3, forty-one had already had their tonsils and adenoids removed when sinusitis was diagnosed. Perhaps they were removed for independent disease before the sinusitis was present, perhaps because they were infected from post-nasal discharge from sinusitis; perhaps because of symptoms which should have directed attention to the sinuses rather than to the tonsils and adenoids themselves. It is even possible that the sinusitis originated in some instances as a result of faulty technique during operation. What of the thirty-five children in this group who still had tonsils and adenoids present? There were remnants from unsuccessful operation in nine of them, and they must be discounted. Consider then twenty-six children with sinusitis, and tonsils and adenoids present. In nine of these they were infected and removed in the course of treatment; in six they were infected but not removed for one reason or another; in eleven they remained healthy; eight of these latter being in children with sinusitis that was cured by treatment, and three in those who improved. Arguments for and against sinusitis as a cause of infection of the tonsils and adenoids can be deduced from these figures.

The writer believes that sinusitis is a common cause of inflammation of the adenoids, and to a lesser degree of the tonsils. The first step in the treatment of sinusitis is the treatment of the sinus itself, and not the removal of tonsils and adenoids. If the latter are infected and fail to respond to such treatment they should be removed. If there is a large pad of infected adenoids interfering with respiration, treatment of co-existing sinusitis is not likely to lead to cure until it is removed.

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TABLE 1.

RECORDS OF 24 CHILDREN IN WHOM MUCUS, MUCO-PUS, OR PUS WAS FOUND ON ROUTINE ASPIRATION OF THE ANTRA OF 1

Series Number.	Sex.	Age.	RIGHT ANTRUM.							LEFT ANTRUM.						
			1st Aspiration. Removal of T.A.	2nd Aspiration. 6 months later.	X-Ray.	No. of Washes. Operation, if any.	Local Result.	1st Aspiration. Organisms Present.	2nd Aspiration. Organisms Present.	1st Aspiration. Removal of T.A.	2nd Aspiration. 6 months later.	X-Ray.	No. of Washes. Operation, if any.	Local Result.	1st Aspiration. Organisms Present.	2nd Aspiration. Organisms Present.
1	F	6	M	M		1	I.S.Q.	Sterile	Pneumococcus	M	MP		1	I.S.Q.	Sterile	Pneumococcus
2	M	5½	MP	MP		4	Clear	Streptococcus	Pfeiffer Sterile	MP	Nil			Clear	Catarrhalis	Sterile
3	M	6	Nil						Sterile	MP	M		1	Improved	Sterile	Sterile
4	M	4½	Nil						Sterile	MP	Nil			Clear	Pneumococcus	Sterile
5	F	8	MP	MP	+	3		Pneumococcus	Influenza	Nil		+			Friedlander Streptococcus Pneumococcus Pneumococcus	
6	F	3½	MP	Nil	+		Clear	Friedlander	Sterile	Nil		+				
7	M	7	Nil		+			Streptococcus		MP	MP	+	4	Clear	Proteus	Proteus
8	F	5	MP	Nil	+		Clear	Streptococcus Proteus	Sterile	Nil		+			Sterile	
9	F	6	MP	Nil	+		Clear	Streptococcus Pfeiffer Sterile	Sterile	Nil		—			Sterile	
10	M	5	Nil		+					MP	M	+	3	Clear	Pneumococcus	Sterile
11	M	5½	MP	MP	+	3	Clear	Pfeiffer	Pfeiffer	Nil		+			Sterile	
12	F	9	Nil					Streptococcus		MP	Nil			Clear	Pneumococcus	Sterile
13	F	7	Nil					Hofmann		MP	Nil	+		Clear	Friedlander	Sterile
14	M	8	MP	M	+	3	Clear	Staphylococcus Pneumococcus Pfeiffer	Staphylococcus	Nil		+			Sterile	
15	F	6½	MP	Nil	+		Clear		Sterile	Nil		+			Sterile	
16	F	8½	Nil		+			Pneumococcus	Pfeiffer	MP	M	+	1	Clear	Pneumococcus Pfeiffer	Pneumococcus
17	M	5	MP	MP	+	3	I.S.Q.	Pfeiffer	Sterile	MP	MP	+	3	I.S.Q.	Pneumococcus Pfeiffer	Pneumococcus
18	M	8½	MP	Nil	+		Clear	Friedlander	Sterile	MP	MP	+	4	Clear	Pneumococcus	Sterile
19	M	7	Nil	Nil	+			Streptococcus Friedlander Pneumococcus	Sterile	MP	M	+	2	Clear	Pfeiffer Friedlander Sterile	Pfeiffer
20	F	11½	P	P	+		I.S.Q.		Pneumococcus	Nil		+				
21	M	7½	MP	M	+	3	Clear	Friedlander		MP	S	+	1	Improved	Catarrhalis Pfeiffer Sterile	Sterile
22	F	8	MP	M	+	1	Improved	Pneumococcus Staphylococcus Pneumococcus	Sterile	Nil		+				
23	M	4	MP	Nil	+		Clear			MP	Nil	+		Clear	Pneumococcus	
24	M	8	Nil					Friedlander Pneumococcus Staphylococcus		MP	Nil	+		Clear	Friedlander Pneumococcus Streptococcus	Sterile

MP = Muco-pus.

P = Pus.

M = Mucus.

S = Serum.

Antrostomy = Intranasal

TABLE 1.

8 WAS FOUND ON ROUTINE ASPIRATION OF THE ANTRA OF 100 CHILDREN UNDERGOING REMOVAL OF TONSILS AND ADENOIDS.

LEFT ANTRUM.				HISTORY.									General Condition.	1935 Observations. Final Result.	X-Ray	
No. of shes. ration, any.	Local Result.	1st Aspiration. Organisms Present.	2nd Aspiration. Organisms Present.	Nasal Discharge.	Colds.	Cough.	Sore Throats.	Cervical Adenitis.	Snoring & Mouth Breathing.	Headaches.	Otitis Media.	Bronchitis Pneumonia.			R.	L.
1	I.S.Q.	Sterile	Pneumococcus	+	+	+	+	—	—	—	—	+	Fair	Not seen since 2nd aspiration. No improvement from T.A.		
	Clear	Catarrhalis	Sterile	+	+	+	—	+	—	+	+	+	Fair	Last seen 1 year after treatment. Nasal discharge did not clear up after T.A. : only after antrum washes.		
1	Improved	Sterile	Sterile	—	—	—	—	—	—	—	+	—	Good	Improved after T.A. and antrum wash later. No further otitis.	—	—
	Clear	Pneumococcus	Sterile	—	—	+	+	+	+	—	—	+	Fair	Antrum cleared up after T.A. without lavage.	+	—
		Friedlander Streptococcus Pneumococcus Pneumococcus		+	+	+	+	—	+	—	+	—	Fair	No improvement from T.A., antrum lavage, antrostomy or convalescent home.	+	+
				—	—	+	+	—	+	—	—	—	Fair	Very well since T.A. No snoring. Very few colds.	—	—
4	Clear	Proteus	Proteus	—	—	+	+	—	+	+	—	—	Fair	Very well now. Generally much improved.	—	—
		Sterile		+	+	+	+	+	+	+	—	+	Poor	Has remained well and free from nasal discharge.	—	—
		Sterile		+	+	—	+	—	—	—	+	+	Fair	Not seen again. Letter 1935 very well and no nasal discharge.		
3	Clear	Pneumococcus	Sterile	—	—	+	—	+	—	—	—	—	Fair	Occasional colds. Otherwise well	—	+
		Sterile		—	—	—	+	+	—	—	—	—	Fair	Free from cough and sore throat (Letter).		—
	Clear	Pneumococcus	Sterile	—	—	—	—	—	+	+	+	—	Poor	Free from sore throats and headaches.	—	—
	Clear	Friedlander	Sterile	+	+	+	—	—	+	—	—	—	Good	No nasal discharge now, except during occasional colds.	—	—
		Sterile		—	—	—	+	—	+	+	—	+	Fair	No further bronchitis. Headaches much improved.	+	+
		Sterile		—	—	+	+	—	+	+	—	—	Fair	Coughs and colds much improved. No snoring.	—	—
1	Clear	Pneumococcus	Pneumococcus	+	+	+	+	—	+	—	—	+	Good	Fewer colds, but apt to have nasal discharge.	—	—
3	I.S.Q.	Pneumococcus	Pneumococcus	+	—	+	—	—	+	—	+	+	Fair	No improvement.	+	+
ostomy		Pfeiffer														
4	Clear	Pneumococcus	Sterile	+	+	+	+	+	+	—	—	+	Good	No nasal discharge, cough or colds. Very well.	—	—
2	Clear	Pneumococcus														
		Pfeiffer	Pfeiffer	—	+	+	+	—	+	—	—	+	Fair	Improved only after washing of antrum for third time.	—	+
		Friedlander		+	—	+	+	—	+	—	—	+	Fair	Did not finish treatment, but is now very well and free from nasal discharge.	+	+
		Sterile		—	—	—	+	—	—	—	—	—	Good	Still gets colds and sore throats (Letter).		
1	Improved	Catarrhalis	Sterile	—	—	+	+	—	+	+	—	—	Fair	Very well 6 months after. Not seen since. Very well 1935, letter.		
		Pfeiffer		—	—	—	+	—	—	—	—	+	Fair	Still gets colds and sore throats (Letter).		
	Clear	Pneumococcus		—	—	+	—	+	+	—	—	—	Fair			
	Clear	Friedlander	Sterile	+	+	—	—	+	+	—	+	—	Fair	No improvement in otitis media. Nose improved.	+	+
		Pneumococcus														
		Streptococcus														

Antrostomy = Intranasal antrostomy.

T.A. = Removal of tonsils and adenoids.



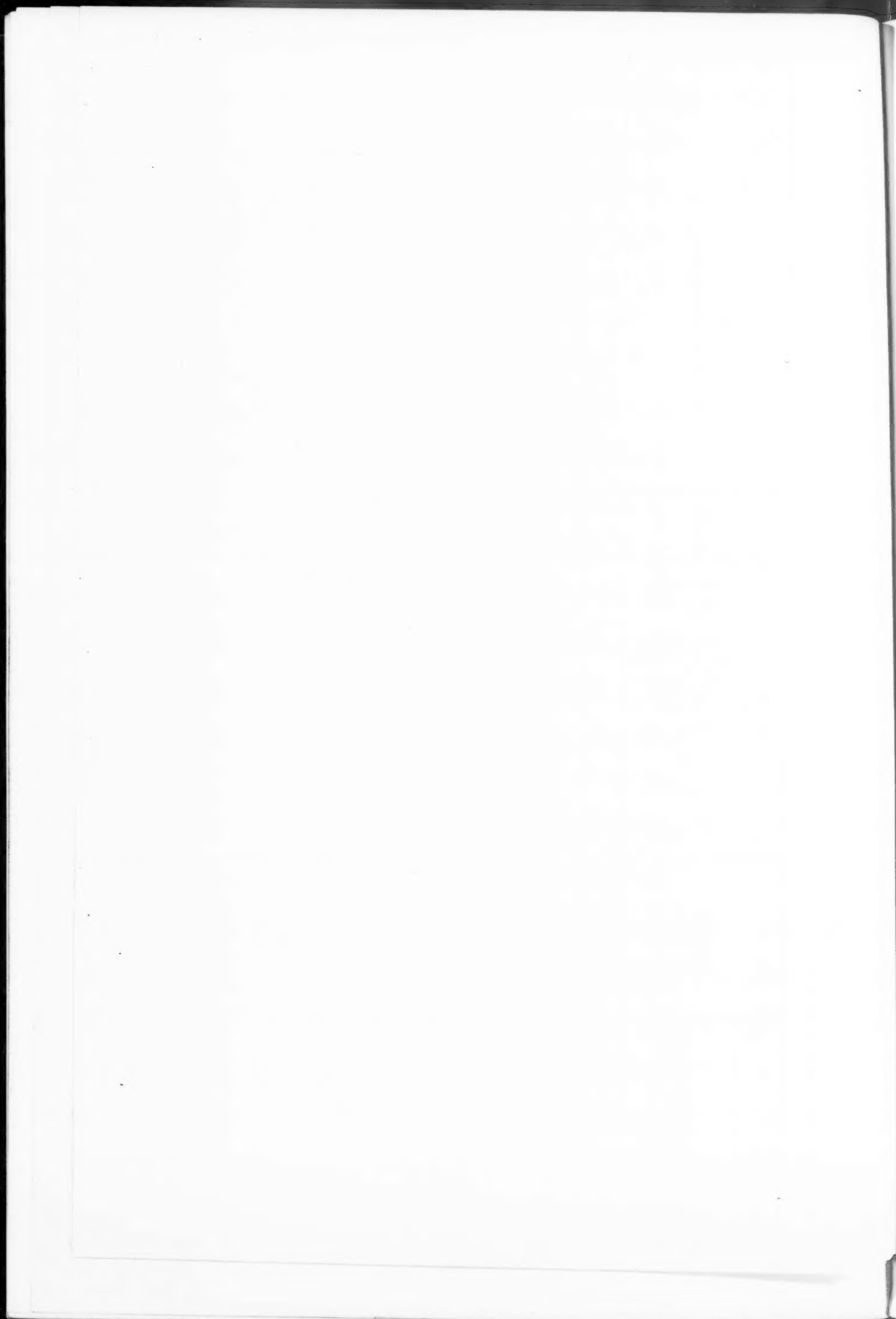
TABLE 3.

RECORDS OF A FURTHER 76 CHILDREN IN WHOM MUCUS, MUCO-PUS, OR PUS WAS ASPIRATED FROM THE ANTRA.

Series Number.	Sex.	Age.	RIGHT ANTRUM.				LEFT ANTRUM.				Condition of Tonsils and Adenoids.	HISTORY.								General Condition.	Observations. Final Result.	X-Ray.	
			Aspiration.	No. of washes. Operation if any.	Local Result.	Organisms Present.	Aspiration.	No. of washes. Operation if any.	Local Result.	Organisms Present.		Colds.	Cough.	Sore Throats.	Cervical Adenitis.	Snoring and Mouth Breathing.	Headaches.	Otitis Media.	Bronchitis. Pneumonia.			R.	L.
25	F	6	MP	2 Antrostomy	Clear	Staphylococcus	Nil			H. Streptococcus	Removed	+	+	+	+	+	+	+	+	Fair	Greatly improved, but still apt to get colds. Right antrum wash clear.	+	—
26	F	3	MP	3 Antrostomy	Clear	Pneumococcus	MP	3	Clear	Sterile	Normal	+	+	+	+	+	+	+	+	Fair	Not seen since three months after treatment. Was then free from nasal discharge.	+	+
27	F	10½	Nil	Antrostomy		Sterile	P	3 Antrostomy	Improved	Pfeiffer	Removed	—	+	+	+	+	+	+	+	Good	Improved after antrostomies. Still apt to catch cold, but no chronic nasal discharge.	+	—
28	F	4½	MP	2	Clear	Streptococcus Viridans Pfeiffer	MP	2	Clear	Pfeiffer	Infected 1933 Infected remnants	+	+	+	+	+	+	+	+	Fair	Improved on washes, but tonsils and adenoids remained unhealthy. They were then removed.	+	—
29	M	11½	MP	2	Clear						Removed 1932	+	+	+	+	+	+	+	+	Fair	? Result of antrum washes or T.A. operation.	+	+
30	F	4½	P	5 Antrostomy	I.S.Q.	Pneumococcus	P	5 Antrostomy	I.S.Q.	Pneumococcus	Removed	+	+	+	+	+	+	+	+	Fair	No improvement from treatment, including one year at sea-side. Has bronchiectasis.	+	—
31	M	10	P	2	Clear	Pneumococcus	P	2	Clear	Pneumococcus	Removed	+	+	+	+	+	+	+	+	Fair	Cleared up completely and permanently after 2 washes. Has had nasal discharge for 3 years.	+	—
32	F	5½	MP	3	Clear	H. Streptococcus	MP	4	Clear	Sterile	Removed	+	+	+	+	+	+	+	+	Good	No nasal discharge. Well locally and generally.	+	—
33	M	7½	P	2	Clear	Sterile	MP	2	Clear		Removed	+	+	+	+	+	+	+	+	Fair	Cough improved. Still snores. Sneezes. ? Allergic rhinitis.	+	—
34	M	10½	Nil				MP	2	Clear	Pneumococcus Streptococcus Friedlander	Inflamed	+	+	+	+	+	+	+	+	Fair	Nasal discharge and sore throats cured. Tonsils not removed.	+	+
35	F	4½	MP	2	Clear	Pneumococcus	Nil				Normal	+	+	+	+	+	+	+	+	Fair	Colds and coughs improved. In 1933 had nephritis with swollen right eye. Right antrum wash clear.	+	—
36	F	9½	P	2 Antrostomy	Clear	Streptococcus Pfeiffer Sterile	Nil				Removed	+	+	+	+	+	+	+	+	Good	Cured by antrostomy.	+	—
37	M	2½	MP	4	I.S.Q.		MP	4	I.S.Q.	Sterile	Enlarged	+	+	+	+	+	+	+	+	Good	Not seen since three months after first treatment.	+	—
38	M	9	MP	2	Clear	Pneumococcus	MP	2	Clear	Pneumococcus	Infected. Removed at time of 1st wash	+	+	+	+	+	+	+	+	Fair	No improvement. Had first antral washes and T.A. done at same time.	+	—
39	M	8½	Nil				MP	3	Clear	Staphylococcus Pfeiffer Sterile	Normal	+	+	+	+	+	+	+	+	Good	Remained free from colds, cough, headaches and nasal discharge since washes.	+	—
40	M	7	MP	3	Clear	Sterile	MP	3	Clear		Removed	+	+	+	+	+	+	+	+	Fair	Very well ever since treatment. Had had nasal discharge for 1 year.	+	+
41	F	6	MP	3	I.S.Q.	Streptococcus Pneumococcus Hofmann	MP	3	I.S.Q.	Streptococcus Viridans	Normal	+	+	+	+	+	+	+	+	Poor	No improvement. T.A. removed 1934. Long course of (Displacement treatment.)	+	—
42	F	7½					M	1		Streptococcus	Normal	+	+	+	+	+	+	+	+	Fair	Had had nasal discharge for 4 years. Cleared up permanently after 1 wash.	+	—
43	M	6	M	4	Clear	Pneumococcus	MP	4	Clear	Streptococcus	Normal	+	+	+	+	+	+	+	+	Fair	Seen in 1933 and not since. One year after washes was clear of symptoms.	+	—
44	F	10	MP	4	Improved	Sterile	MP	4	Improved	Pneumococcus Pfeiffer	Removed	+	+	+	+	+	+	+	+	Fair	Did not improve by washing. Given autogenous vaccine and improved greatly. Apt to get colds.	+	+
45	M	5	MP	5	I.S.Q.	Sterile	MP	2	I.S.Q.		Adenoid remnants	+	+	+	+	+	+	+	+	Poor	Frequent colds and snoring followed T.A. operation 1 year previously. No benefit from washes or vaccines.	+	+
46	M	9	MP	3	Clear	Pneumococcus	MP	2	Clear	Pneumococcus	Removed	+	+	+	+	+	+	+	+	Good	Improved only temporarily. Now has nasal discharge again. Antral washes 1935. M.P. both sides.	+	+
47	M	7	P	3 Antrostomy	Improved	Staphylococcus	MP	Antrostomy	Improved		Removed	+	+	+	+	+	+	+	+	Fair	Improved for 2 years. Nasal discharge occurred. Antrostomy both sides 1935. Improved.	+	+
48	F	11	MP	4	Clear	Pneumococcus	MP	4	Clear	Pneumococcus	Removed	+	+	+	+	+	+	+	+	Poor	Had had nasal discharge for many years. Cleared up by washing. General condition still poor.	+	—
49	F	6	MP	1		Pneumococcus	Nil				Inflamed	+	+	+	+	+	+	+	+	Fair	Seen in 1933. Letter received 1935. Has remained well ever since. One wash.	+	—
50	M	5	MP	1		Pneumococcus	MP				Scarred remnants	+	+	+	+	+	+	+	+	Fair	Six months nasal discharge cleared by one wash. T.A. remnants removed six months later.	+	—
51	F	10	MP	3 Antrostomy	I.S.Q.	Pneumococcus	Nil	(Antrostomy)		Sterile	Removed	+	+	+	+	+	+	+	+	Fair	No improvement. In 1934 discharge from both sides of nose. Bilateral antrostomy. Improved.	+	—
52	F	5½	MP	4	Clear	Sterile	MP	2	Clear		Removed	+	+	+	+	+	+	+	+	Good	Nasal discharge followed T.A. operation 2 years previously. Cured by washes.	+	—
53	F	12	MP	2	Clear	Staphylococcus	Nil				Infected. Removed at time of 1st wash	+	+	+	+	+	+	+	+	Good	Very little improvement from washes and T.A. operation. Left antrum became infected in 1935.	+	—
54	F	8	MP	1		Pneumococcus	MP				Normal	+	+	+	+	+	+	+	+	Good	Free from symptoms since antrum wash.	+	—
55	F	7½	P	2	Clear	Pneumococcus Pfeiffer	MP				Normal	+	+	+	+	+	+	+	+	Fair	Colds better. Headaches which were bad have not recurred since washes.	+	—
							MP				Normal	+	+	+	+	+	+	+	+	Fair	Nasal discharge of 3 years duration permanently clear.	+	—

Colds better. Headaches which were bad have not recurred since washes.

Nasal discharge of 3 years duration permanently clear.



CREATINE METABOLISM AND THE GONADS

BY

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AND

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It has long been recognized that endogenous creatine is a normal constituent of the urine of the infant and the child, whereas in the adult, unless in the female during pregnancy and the first few days of the puerperium, no creatine is excreted in the urine. Although it has been apparent that this change in metabolism occurs about the time of puberty, and it has been surmised that it may be associated with the activity of the gonads, there is not extant any sufficiently long series of observations demonstrating the fact conclusively. It is for this reason—to determine the exact age at which this change takes place and to correlate it if possible with sexual development—that the following investigation was undertaken. In the series of cases investigated, children of all ages and of both sexes from infancy till after puberty are included. Unfortunately, however, owing to the fact that it is difficult to accommodate boys of the older ages in a children's hospital the numbers of males about puberty are relatively small, but this would seem in no way to detract from the conclusiveness of the results.

Methods.

The children studied were confined to bed in hospital so that the diet and the urinary output could be controlled. They were given the following standard diet during the whole course of the investigation:—

Bread, butter, marmalade, eggs, vegetables and fruit with milk which was restricted to 10 oz. per day for all the children except the infants. (No meat, fish, meat extracts, fowl or cheese allowed.)

It must, of course, be appreciated that milk contains a small amount of creatine (9 to 10 mgm. per cent.) but this is probably not more than the average individual can metabolize. After two preliminary days on this diet the total urine was collected and three successive twenty-four hours' specimens, i.e., those of the third, fourth and fifth days, were examined for creatine and creatinine according to Folin's method. The daily averages are recorded in the accompanying tables.

TABLE 1.
AVERAGE CREATINE EXCRETION IN TWENTY-FOUR HOURS.

BOYS.

CASE No.	AGE	WEIGHT KGM.	CREATININE EXCRETION MGM.	CREATINE EXCRETION MGM.	REMARKS
1	7 mth.	5	80	95	
2	7 "	5.5	84	119	
3	8 "	6.1	78	113	
4	1 yr.	9	97	105	
5	1 " 6 mth.	10.9	144	115	
6	1 " 11 "	9.1	152	120	
7	4 " 8 "	30.4	365	153	
8	5 " 1 "	17.2	271	173	
9	5 " 1 "	17.1	254	127	
10	7 " 9 "	25	459	143	
11	8 " 5 "	34.5	653	127	
12	12 "	54.5	839	none	
13	12 " 6 mth.	63.3	752	145	
14	12 " 8 "	41.4	764	none	
15	12 " 9 "	35.7	655	none	
16	12 " 10 "	77	1253	none	
17	13 "	37.7	735	none	
18	13 " 1 mth.	49.1	870	none	very well developed
19	13 " 5 "	50.4	755	90	
20	13 " 5 "	75	940	160	
21	13 " 6 "	34.5	422	none	

TABLE 2.

GIRLS.

1	1 yr. 11 mth.	9.1	179	100	
2	3 " 7 "	11.1	147	92	
3	5 " 3 "	27.3	436	86	
4	6 " 6 "	15.5	237	95	
5	7 "	22.6	438	145	
6	8 " 6 mth.	22.1	350	117	
7	9 " 11 "	25.5	444	74	
8	11 " 10 "	33.6	722	61	
9	11 " 11 "	32.7	645	none	menstruated
10	12 "	44.5	802	none	menstruated
11	12 "	37.7	715	75	
12	12 " 2 mth.	64	927	184	
13	12 " 6 "	41.2	646	90	
14	12 " 6 "	65	1006	none	menstruated
15	12 " 6 "	51.4	816	77	
16	12 " 6 "	51	831	none	menstruated
17	12 " 7 "	73.1	923	none	menstruated
18	12 " 7 "	37.7	817	77	
19	12 " 8 "	73.6	1040	none	menstruated
20	12 " 9 "	33.9	625	98	
21	12 " 10 "	64.7	951	none	menstruated
22	13 "	38.2	778	none	menstruated
23	13 "	77	1252	none	menstruated
24	13 " 2 mth.	55.9	925	none	
25	13 " 3 "	77	1231	none	menstruated
26	13 " 5 "	39.5	726	none	menstruated
27	13 " 10 "	38.2	790	79	

From the above tables it would appear that the age at which creatinuria ceases varies between twelve and fourteen years. Of the total forty-eight children twenty-nine were within these limits, nineteen being girls and ten boys. Of the nineteen girls twelve did not excrete creatine, and all of them, with one exception, had already menstruated. It will be noted that the majority of the girls at this age period who still passed creatine in the urine were nearer the age of twelve than fourteen years. Of the ten boys over twelve years only three (table 1, no. 13, 19, 20) still passed creatine in the urine. These three boys showed normal sexual development although no pubic hair was present. One striking feature of the findings is the absence of any correlation between the age of the child and the degree of creatinuria. There is no gradual decline in the creatine excretion, as might have been expected, but a more or less sudden disappearance which, as above noted, usually takes place between twelve and fourteen years of age.

Discussion.

Various theories have been brought forward to explain the presence of creatine in the urine of the child and its absence from the urine of the adult. Powis and Raper¹ believe that the explanation lies in the inability of the immature muscles during growth to utilize or metabolize creatine into creatinine. There is no doubt that muscle is essential for the conversion of creatine into creatinine, and in cases where there is much muscular degeneration, e.g., muscular dystrophy, as noted by MacCrudden and Sargent², Gibson, Martin and Buell³ and Janney, Goodhart and Isaacson⁴, creatinuria may persist well into adult life, even to the age of forty-eight years. But the conception that immature muscle is incapable of causing this conversion is unlikely, since the condition of creatinuria does not, as has been noted above, gradually diminish but ceases more or less abruptly.

Rose⁵ in 1911, as the result of a series of examinations of children and adolescents, noted that 'creatine is usually present in the urine until or after the age of puberty,' and he was probably the first to suggest any influence of the gonads on creatine metabolism. Rose found creatinuria in both boys and girls at the age of fifteen years, but none in any child over this age. There are, however, no girls between the ages of fifteen and twenty years, and no boys between fifteen and seventeen years in his series, so that the exact age of the disappearance of creatinuria and the relationship of this to puberty is somewhat indefinite. Moreover, it should also be pointed out that the subjects in Rose's series were on a general diet, and hence his findings leave doubt regarding the endogenous or exogenous source of the creatine present in the urine.

The decisive influence of the sex glands on the excretion of creatine is strongly supported by the findings of Remen⁶. This worker showed that, (1) very old people excrete a small amount of creatine even on a creatine-free diet, and that their creatine tolerance was greatly diminished; (2) a

eunuchoid person had a constant creatinuria and a low creatine tolerance; (3) a man with a 'pituitary obesity' and hypogenitalism had a pronounced creatinuria; and (4) a man who was castrated for carcinoma of the penis reacted like the eunuchoid.

MacNeal⁷ also found creatinuria in eunuchoids. Buchler⁸ mentions a girl of eight years with precocious sexual development who reacted like an adult in that no creatine was found in the urine on a creatine-free diet. These findings—the reappearance of creatine in the urine of people whose sexual function has ceased, either through operation or old age, and its premature disappearance in children with precocious sexual development—certainly support the idea that the really determining factor in the utilization of creatine is the activity of the gonads. Indeed, it would seem that only on this basis can be satisfactorily explained the persistence of creatinuria during infancy and throughout childhood, and its more or less sudden disappearance at puberty.

Thanks are due to Dr. Leonard Findlay for his valuable suggestions and his kind help in the preparation of this communication.

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INFANTILISM WITH BONY CHANGES RESEMBLING RICKETS AND CALCI- FICATION IN KIDNEYS

BY

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The following case is reported because it shows unusual features:—

R. R. first came under observation on January 12, 1934, at the age of two years, when he was admitted to Alder Hey Hospital with the complaint that he was unable to walk. He was the fifth child of healthy parents. One child had died of measles; the others were reported to be well. The patient's birth had been normal, with an easy confinement and



FIG. 1.—R. R., 1.2.34. Skiagram of wrist.

the birth weight was eight pounds. Up to the age of ten months he appeared to be developing normally, but from this time onwards he ceased to grow. He began to walk at the age of twelve months, but three months later he 'went off his feet,' and crawled about the floor until his first admission. His teeth appeared early, but his mother could not remember the exact dates of dentition. He was fed on dried milk until eleven months old and

then on condensed milk for a month. After this he was given a mixed diet. Three teaspoonsful of cod-liver oil emulsion were given daily from the age of eleven months to the age of seventeen months.

ON EXAMINATION he was found to be small and under-nourished, weighing only 17 lb. His height was 2 ft. 8 in. His anterior fontanelle was closed and primary dentition was complete. There was no deformity of the



FIG. 2.—R. R., age 3 years, 4 months.

chest, but a slight degree of genu valgum was present. The epiphyses were enlarged and radiological examination of his wrists showed the presence of active rickets (fig. 1). He was treated with cod-liver oil (3,000 international units of vitamin D daily), and ultra-violet light (one minute increasing to twenty minutes at a distance of 22 inches) three times a week. Radio-

logical examination of the radial epiphyses at the end of a month showed a very slight attempt at healing. He then developed an acute febrile attack, for which he was isolated. His parents removed him on their own responsibility on February 6, 1934.

He was re-admitted on May 25, 1935, again with the complaint of not being able to walk. On examination he was found to be still underweight, weighing only 18 lb. 8 oz. at the age of three years, four months (fig. 2). Radiological examination showed the presence of active rickets, and of a fractured left ulna. The child developed broncho-pneumonia four days after admission, from which he recovered entirely in three weeks. On June 15, 1935, he was found to have a fracture of the right humerus.

The fractures were treated by means of suitable splints, and 3,000 units vitamin D were given daily in the form of an oily solution of calciferol.



FIG. 3.—R. R., 8.7.35. Skiagram of wrist.

Ultra-violet light (one minute, increasing to twenty minutes, at a distance of 22 inches) was given three times a week. The treatment was continued for five months, but no radiological healing of the epiphyses occurred (fig. 3). The following investigations were then carried out:—

29.10.35.	BLOOD UREA	20	mgm. per 100 c.c.				
15.11.35.	„ „	21	„ „	100 c.c.			
8.11.35.	BLOOD CALCIUM	7.27	„ „	100 c.c.	BLOOD PHOSPHORUS	6.25	mgm.
17.11.35.	„ „	7.52	„ „	100 c.c.	„ „	4.75	„
16.1.36.	„ „	10.85	„ „	100 c.c.	„ „	2.17	„
21.4.36.	„ „	8.0	„ „	100 c.c.	„ „	4.16	„
21.4.36.	BLOOD PHOSPHATASE	2.94	units.				



FIG. 4.—R. R., 22.11.35. Skiagram of kidneys.



FIG. 5.—R. R., 21.4.36. Skiagram of kidneys.

- 17.1.36. CALCIUM BALANCE.
 Total intake of CaO in twenty-four hours 1,124.4 mgm.
 „ output „ „ „ „ „ 961.6 „
 Retention „ „ „ „ „ „ 162.8 „
- 12.11.35. FAT CONTENT OF FAECES.
 Unsplit (neutral fat) ... 3.88
 Split fat ... 17.15 } per cent. of dried faeces.
 Total fat ... 21.0 }
- 29.5.36. ALKALI RESERVE 50.2 vol. CO₂ per 100 c.c.
 URINE EXAMINATIONS. Specific gravity averaged 1006.
 Albumin and sugar were never found.
 An occasional leucocyte was seen in the deposit.
 Casts were not found on any occasion.
 THE WASSERMANN REACTION of the blood was negative.
 THE MANTOUX REACTION (1/1000) was negative.



FIG. 6.—R. R., 6.4.36. Skiagram of wrist.

THE BLOOD COUNT:—

No. of Red cells	2,300,000 per c.mm.	Differential count.	
„ White cells	7,000 „ „	Small mononuclears	57 per cent.
Haemoglobin ...	40 per cent.	Large „	5 „ „
		Polymorphonuclears	35 „ „
		Eosinophils	2.7 „ „
		Mast cells3 „ „

- 22.11.35. RADIOLOGICAL EXAMINATION (fig. 4 and 5) of renal tract showed small areas of calcification scattered throughout the kidney substance.

PROGRESS. The general condition of the child improved; he looked better, grew more cheerful and gained weight. Anti-rachitic treatment (ultra-violet light and added vitamin D) was discontinued when the renal calcification was discovered, but he was allowed a liberal diet. Daily

massage and exercises were given, and as a result of this treatment he learned to walk and was soon able to progress unassisted around the ward. His blood picture became normal after administration of iron by mouth, but serial radiographs of his radial epiphyses showed little, if any, improvement, and on May 15, 1936, he fell and re-fractured his right humerus (fig. 6 and 7).



FIG. 7.—R. R. 15.5.36. Skiagram of humerus.

Discussion.

It is difficult to determine the nature of the underlying disturbance which has been responsible for the infantilism, the renal calcification, and for the presence of 'rickets,' which has failed to respond to treatment with adequate doses of vitamin D and ultra-violet light.

The following conditions have to be considered as possible causes:—

(1) Lack of vitamin D and sunlight. That the rickets cannot be due solely to vitamin D deficiency is shown by the fact that after five months' treatment no healing took place. The renal calcification suggests that while absorption of calcium from the intestine was adequate, normal redistribution and utilisation in the body did not take place; thus calcium would be deposited in the kidneys during concentration of urine containing excess of calcium salts.

(2) 'Renal rickets.' The fact that the bone changes are associated with infantilism suggests this as a possible diagnosis, but the biochemical findings do not support it. The renal function is normal and the blood phosphorus has never reached a high figure.

(3) Coeliac disease. This, too, would account for the presence of infantilism and bony changes resembling rickets. The child, however, does not present the clinical features associated with coeliac disease, nor does the analysis of the stools bear out such a diagnosis.

(4) Acidosis. Lightwood¹ recently reported a case of renal calcification associated with acidosis. There is no evidence that this is a causal factor here. The alkali reserve estimated by van Slyke's method, is normal.

(5) Parathyroid hyperplasia. It is possible that hyperplastic changes have occurred in the parathyroids, which prevent the healing of the rickets. The blood calcium, however, has never reached a high level.

No single factor seems to offer an adequate explanation of the condition. It is possible that a deficiency of vitamin D and a hyperplasia of the parathyroids are both concerned. Experimental work has shown that the parathyroids hypertrophy when the diet is deficient in calcium. Luce² found that rats fed on a diet deficient in calcium, show a consistent enlargement of the parathyroid gland, and concludes that the parathyroids are making an attempt by an increase in normal functioning cells to supply a metabolic need, arising from calcium deprivation. She says: 'The nature of this need is not proven, but it may be that in the absence of calcium the organism is unable to make full use of the growth factor in diet.' Erdheim³ has described an enlargement of the parathyroid gland in spontaneous rickets in rats, and Pappenheimer⁴ has described enlargement of the gland with hyperplasia of cells in human rickets. Ritter⁵ also has reported increased connective tissue, hyperaemia and oedema in the parathyroids of rachitic children. Langmead and Orr⁶ have described changes in the parathyroids secondary to renal rickets.

Conclusion.

The case does not present an uncomplicated clinical picture. Any explanation must be in the nature of a hypothesis. It may be, that, the rickets having remained untreated for a year, the child was in a state of calcium deprivation owing to failure of absorption, and hence parathyroid hyperplasia occurred. When calcium was restored to the child by the administration of vitamin D and ultra-violet light, in addition to a good

diet, the over-activity of the parathyroids prevented calcium from being laid down in the bone and caused its deposition in the kidneys during concentration of the urine.

Summary.

A case of infantilism with renal calcification and bony changes resembling rickets, which failed to heal completely under anti-rachitic treatment, is described. The biochemical investigations are recorded. It is shown that the case cannot be explained by vitamin D deficiency, disordered renal function, coeliac disease, acidosis or parathyroid hyperplasia alone. Parathyroid hyperplasia secondary to unhealed rickets, persisting after the exhibition of vitamin D, is suggested as a possible cause.

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CASE REPORTS

SOLITARY CYST OF THE LIVER IN A CHILD AGED FOUR MONTHS

BY

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The literature on the subject of solitary non-parasitic cyst of the liver is now extensive but the occurrence of such a cyst in a child aged four months is sufficiently uncommon to justify the publication of the following case.

J.C., a boy, aged four months, was admitted to the Royal Hospital for Sick Children, Glasgow, in August, 1934, with the diagnosis of 'ascites of unknown origin.' The child weighed $10\frac{1}{2}$ lb. at birth and was fed on the bottle. At the end of a fortnight it was noticed that the abdomen was more prominent than usual although the child was otherwise well. The abdomen continued to increase in size and by the end of eight weeks was greatly distended and tense. At this time vomiting began after every feed and constipation was troublesome, and as treatment gave no relief the child was finally admitted to the hospital at the age of three-and-a-half months. On admission the child appeared somewhat dehydrated but bright and contented, his weight being 25 per cent. over the expected weight. He took his feeds fairly well with occasional vomiting and the stools although infrequent were normal. The abdomen was greatly distended and so tense that accurate palpation was difficult. The percussion note was uniformly dull except in the left iliac fossa and the left hypochondrium. The dullness was continuous with the liver dullness and did not alter with change of position. X-ray photographs showed the presence of a uniform shadow occupying almost the entire abdomen and pelvis, the stomach lying high in the left hypochondrium and the bowel in the left iliac fossa. The abdomen was tapped and 240 c.c. of fluid withdrawn. This fluid was pale, clear, straw-coloured, and was negative to tests for urine and bile. Microscopic examination showed the presence of some red blood corpuscles, and few lymphocytes and epithelial cells. On culture no growth was obtained.

Laparotomy was decided upon and, to lessen the risk of collapse from too sudden release of pressure, fluid was removed from the abdomen for three days prior to operation. The abdomen was opened under ether anaesthesia and an enormous cyst was found filling most of the abdominal cavity and arising from the right lobe of the liver. An attempt to empty the cyst by aspiration failed owing to the presence of numerous loculi. As the cyst wall was continuous with the liver, removal did not seem possible and accordingly the wall was cut through close to the liver and the cut edge sewn with cat-gut to stop the oozing. The liver, gall-bladder and ducts, and other abdominal organs appeared normal and the abdomen was closed without drainage. Recovery was uneventful and the child is now well and thriving.

PATHOLOGICAL INVESTIGATION. The cyst wall and a small piece of liver were sent for examination and the pathologist reported as follows:— '(1) CYST WALL. No epithelial lining can be seen. The wall is composed of fibrous tissue in which numerous dilated bile ducts and some liver cells are present. The cyst is probably of bile-duct origin. (2) LIVER. Histologically the liver shows slight interstitial fibrosis.'

Discussion.

Of the cases of solitary non-parasitic cyst of the liver now recorded in the literature, the majority have occurred in adults, less than half a dozen being within the first decade of life. The present case seems to be the youngest living patient recorded. Owing to the lack of histological and other detail in the recorded cases the origin and etiology of these cysts remains as yet obscure though many theories and suggested classifications have been put forward from time to time. There is general agreement that the majority are congenital in origin, the few described as acquired being degeneration or retention cysts associated with cirrhosis of the liver and a few examples of cystadenomata. Of those described as congenital in origin the following deserve recognition: (1) dermoids; (2) cysts lined with ciliated epithelium presumably derived from the original lining of the primitive fore-gut; (3) lymphatic cysts due to congenital dilatation of the ducts or retention cysts following congenital stenosis; (4) bile-duct cysts produced in the same way as the lymphatic cysts; (5) small multiple cysts associated with polycystic disease of the kidneys; (6) cysts of blood-vessel and endothelial origin. The present case seems to have been of bile-duct origin.

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MASSIVE ATELECTATIC BRONCHIECTASIS ASSOCIATED WITH BRONCHIAL STENOSIS

BY

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AND

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The application of thoracic surgery in children must eventually contribute to the knowledge of the pathogenesis of bronchiectasis. In this report clinical and pathological data concerning a case in which pneumonectomy was performed are presented.

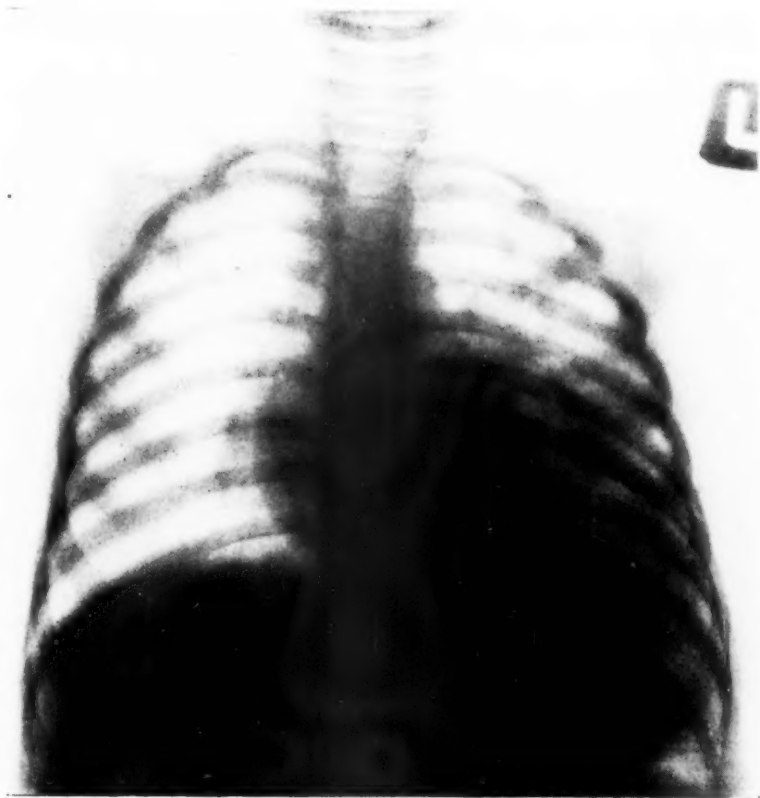


FIG. 1.—Patchy consolidation of the left lung during resolution of the pneumonia in 1933.

F. B., a boy, aged five years, was well until 1933 when he had an illness diagnosed as pneumonia. The pulmonary lesion gradually resolved and an x-ray photograph taken later showed a patchy consolidation of the left lung, but no evidence of collapse (fig. 1). He recovered from this illness and was well until January, 1936, when he had a similar episode. Subsequently he

had a cough which was for a time associated with a little sputum and breathlessness. Later the cough was unproductive. There were no malaise, fever or other constitutional symptoms. In May, 1936, he was admitted to Westminster Hospital for investigation. On clinical examination it was noted that he was a well-nourished, lively child of good colour with slight clubbing of the fingers. The temperature was normal and there was only occasional cough without sputum. Meunier's method of searching for tubercle bacilli by gastric lavage gave negative results. The left side of the thorax showed restricted movement, complete dullness on percussion, medium-pitched bronchial breathing, and whispering pectoriloquy. The right border of the heart could not be percussed, and the cardiac apex lay opposite the fifth rib in the left mid-axillary line.

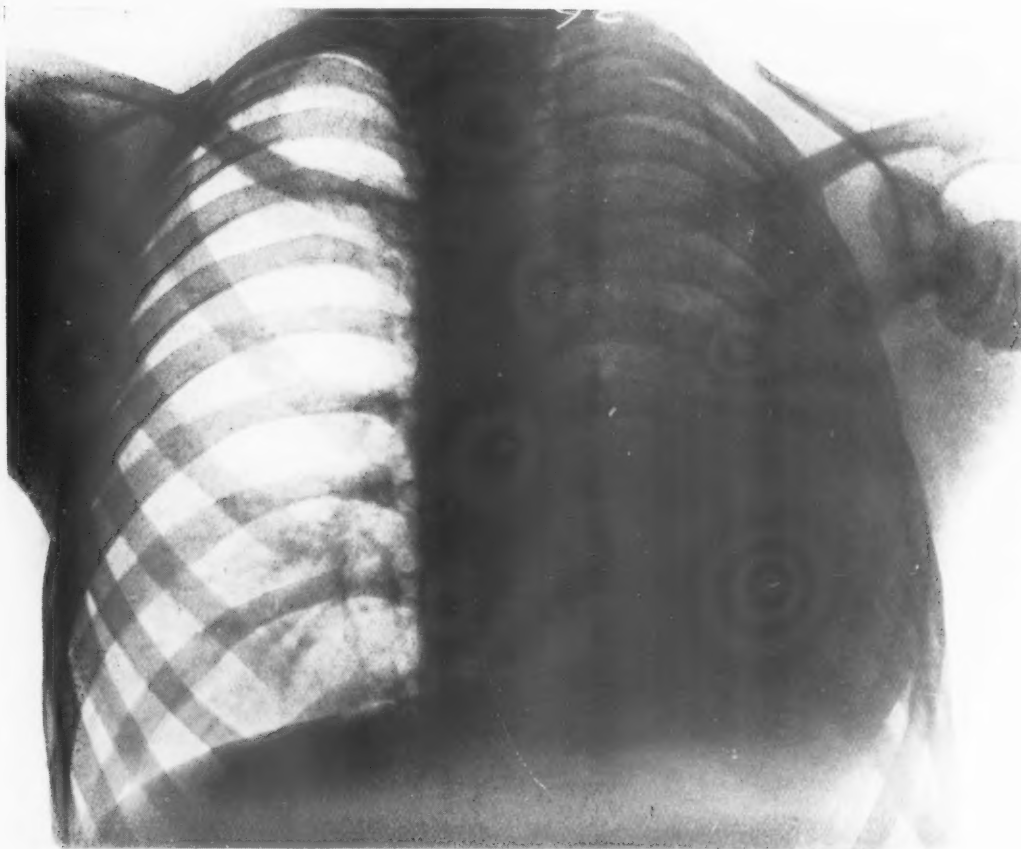


FIG. 2.—Plain skiagram taken on admission.

X-ray examination showed that the left thorax was opaque from apex to base and small, scattered, calcified foci (not visible in the reproduction) were seen in the upper lobe (fig. 2). In view of a strongly positive intracutaneous tuberculin test (1 in 1,000 old tuberculin) it was thought that tuberculosis might be either the underlying or a contributing factor. The displacement of the mediastinum towards the affected side (fig. 2) seemed to rule out the diagnosis of epituberculosis or effusion. The presence of fluid was further excluded by thoracentesis which also demonstrated a greater negative pressure than normal on the affected side. There was no leucocytosis and the sedimentation rate was not increased.

At this stage of the investigation the diagnosis was an interesting one, and it appeared probable there might be a massive collapse or a fibroid lung; the presence of bronchiectasis was suspected and tuberculosis could not be excluded.

Bronchoscopy (Mr. F. C. Ormerod) revealed narrowing of the left main bronchus just proximal to the opening of the left upper lobe bronchus. No secretion was seen in the bronchus and beyond the stenosis the bronchi appeared to be normal. Bronchography with lipiodol then provided evidence of the greatest importance in the elucidation of the case (fig. 3 and 4). The trachea was displaced to the left. The opaque oil entered the bronchi on the left side and demonstrated cylindrical bronchiectasis, but did not penetrate far into the lung, showing that the lung parenchyma was not aerated. There was also much distortion of the bronchi. The first division of the right lower main bronchus was directed into the left side of the chest, showing herniation of the mediastinum by the right lower lobe. A partial stenosis of the left main bronchus was seen about one inch from the bifurcation.

Treatment

In consultation with Dr. Donald Paterson and Mr. Tudor Edwards it was decided that pneumonectomy should be performed. This decision was made because it was felt there was much risk of repeated infection taking place in a functionally useless lung. At operation Mr. Tudor Edwards found the lung to be extremely shrunken and adherent. The structures in the root of the lung were secured by mattress sutures and no enlarged glands were noted. After operation shock was counteracted and a blood transfusion performed. In the post-operation phase there was considerable pyrexia, attributable to infection of blood clot in the left thorax. Eventually the fever disappeared and healing began to take place satisfactorily. The general condition at the present time is excellent.

Pathological report

The specimen of the left lung removed at operation was fleshy and fibrous and contained numerous areas of calcification (fig. 5). Some of the bronchi showed dilation together with massive peribronchial fibrosis. Examination of the left main bronchus showed that the stenosed portion had been left behind in the ligatured stump.

Microscopic sections from various parts of the lung revealed marked peribronchial fibrosis and dilation of the bronchi. There was also dense lymphocytic infiltration chiefly around the bronchi. The alveoli were for the most part collapsed, although many contained blood. Some areas showed dense calcium deposits well circumscribed and encapsulated. Serial sections taken through one area suspicious of a tuberculous process, finally revealed a giant cell of the Langhans type with a surrounding area of epithelioid granulation tissue and lymphocytes (fig. 6 and 7). This histology was suggestive but not diagnostic of tuberculosis.

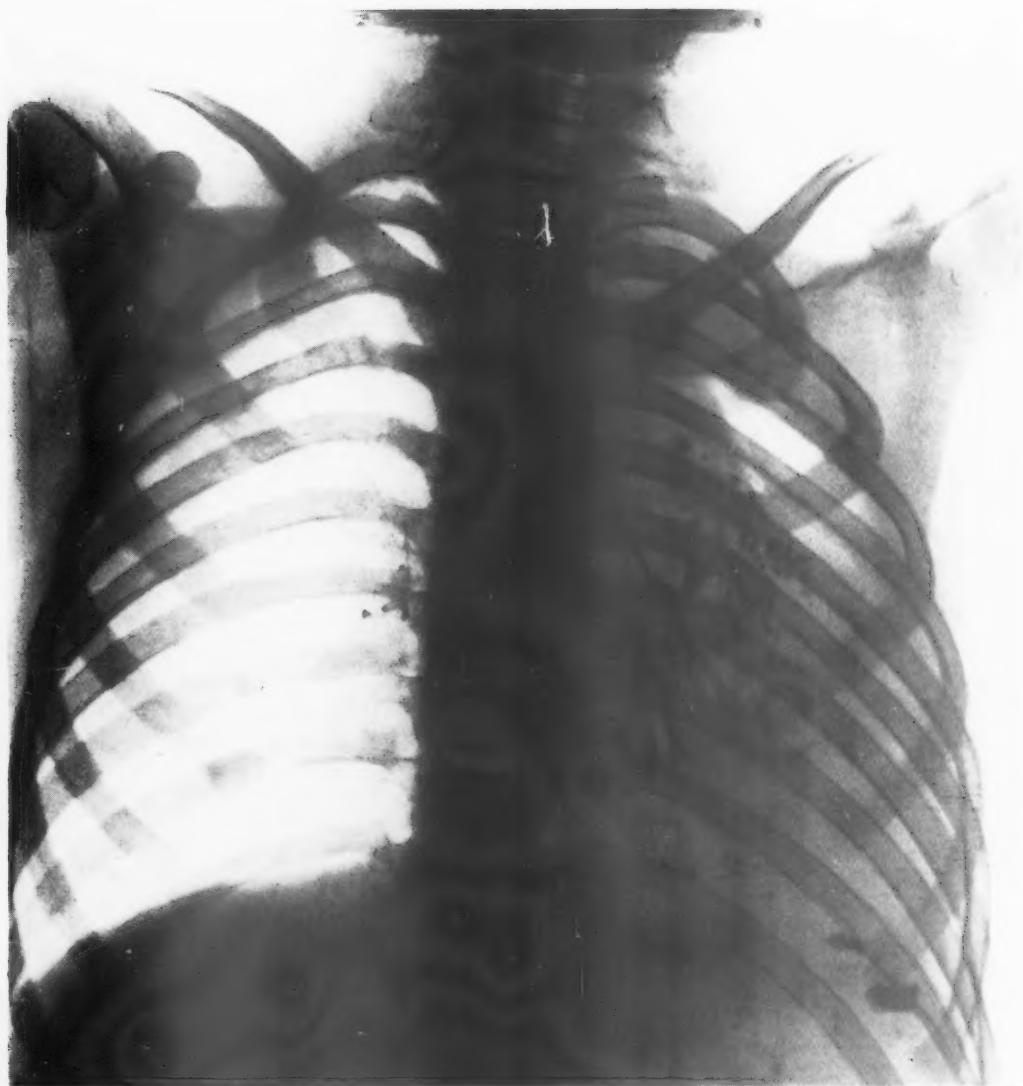


FIG. 3.

Two x-ray photographs taken at different times after lipiodol, showing displacement of the trachea to the left, cylindrical bronchiectasis and stenosis of the left main bronchus. In fig. 4 note the first division of the right lower main bronchus is directed into the left side of the chest showing herniation of the mediastinum by the right lower lobe.

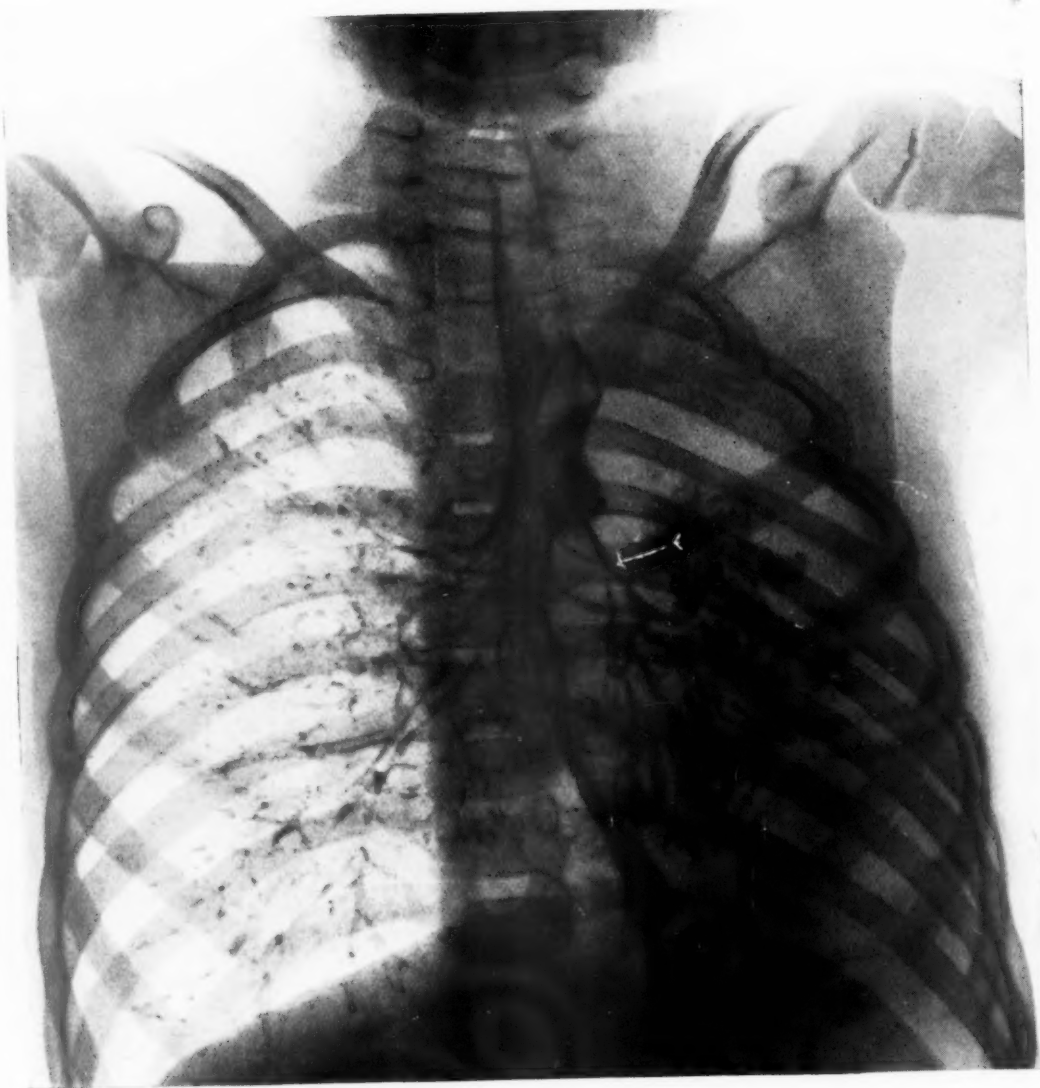


FIG. 4.

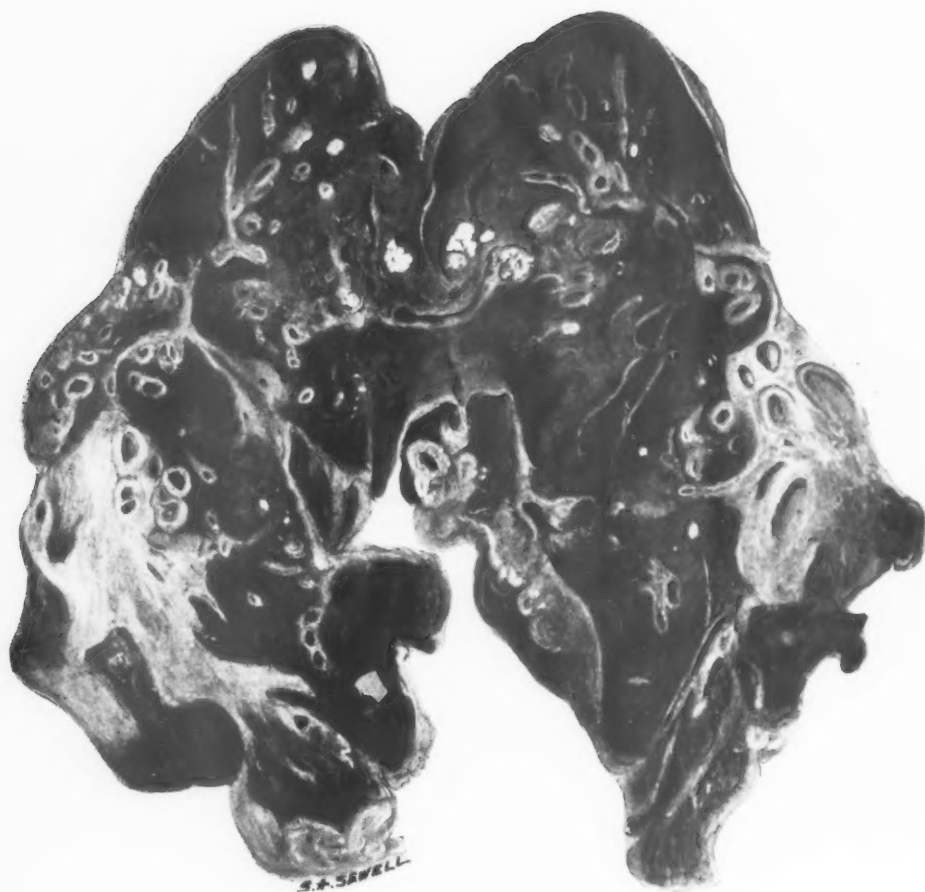


FIG. 5.—Left lung removed at operation showing both cut surfaces. Note areas of calcification, peribronchial fibrosis and bronchial dilatation.

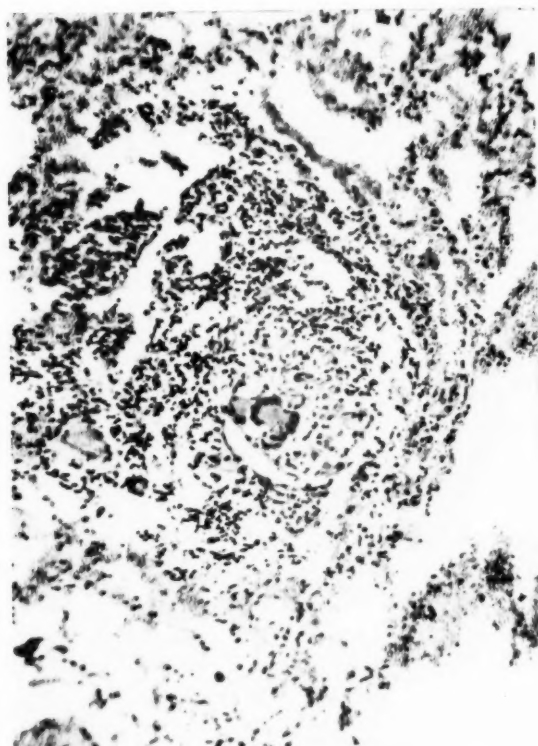


FIG. 6.—Microphotograph of lung containing an area resembling a tubercle.

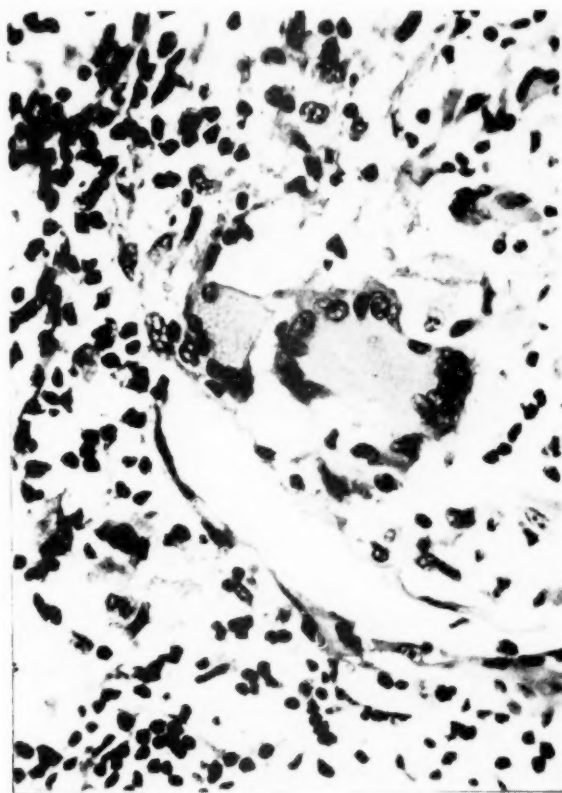


FIG. 7.—High power magnification of fig. 6 showing giant cell of Langhans type.

Discussion.

Both etiologically and pathologically the interpretation of this case is difficult. The important points are the finding of a fibrotic and bronchiectatic lung in a patient in whom the tuberculin test is strongly positive. In children, tuberculosis is not usually regarded as a cause for widespread bronchiectasis. It may be remarked that Wallgren¹ has described a localized and benign form of bronchiectasis occurring at the site and after the healing of a primary focus. There can be little doubt that tuberculosis of the 'childhood type' leads to varying degrees of induration and fibrosis, and it is a point worth considering if this type of tuberculosis may also contribute in the etiology of certain cases of bronchiectasis. The evidence available concerning the present case does not permit a final conclusion; the microscopic and histological findings, though suggestive of tuberculosis are not conclusive.

Another important positive finding in this case is the partial stenosis of the main left bronchus. It is not possible to say what caused this stenosis, though its presence might be an explanation for the failure of the left lung to expand and recover after the pulmonary infections which from the history are known to have taken place. The stenosis itself may have resulted from an ulcerative bronchial lesion or from the effects of a caseous gland in its neighbourhood.

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